

ABSTRACTS OF WORLD MEDICINE

VOL. 10 No. 5

NOVEMBER, 1951

Hygiene and Public Health

1744. The Mortality in Australia from Cancers Peculiar to the Female

H. O. LANCASTER. *Medical Journal of Australia* [Med. J. Aust.] 2, 1-6, July 7, 1951. 3 figs., 6 refs.

Most of the information used in this statistical review has been taken from the records of female deaths attributed to carcinoma of the breast, uterus, ovaries, vagina, and vulva in Australia during the years 1908-45, as published in the annual bulletin of the Bureau of Census and Statistics, Canberra. Although cancer of the uterus in recent years has been officially subdivided into cancer of the body and cancer of the cervix, this subdivision has been disregarded, as, in the opinion of the author, it is unlikely to be reliable. It is pointed out that a small error may have been introduced in early years, since it is probable that some deaths attributed to "cancer of the abdomen" were due to cancer of the ovaries, and that others attributed to "cancer of the pelvis" were due to cancer of the ovaries or uterus; in each case, however, the numbers involved are said to be relatively small.

A short introductory review of mortality in females from cancer of all sites in Australia during the period 1932-4 stresses the importance of the cancers peculiar to women. The author states that "if a group of females was followed throughout their life, it would be expected that of all the various sites of cancer the stomach would claim the greatest number of victims, being followed closely by the breast, the intestines (excluding the rectum), and the uterus". Moreover, the incidence of cancer of the breast and of the genital organs tends to be greater among younger women than does that of cancer in other sites. Thus over the whole period 1908-45 female deaths due to cancer of the breast and to cancer of the genital organs together accounted for about 50 to 60% of all female deaths from cancer in the age group 25 to 54 years, and this proportion decreased with increasing age to about 25% at age 75 years and over.

The main discussion is based on two tables showing mortality rates for cancer of the breast and cancer of the uterus separately among women in the age groups 0 to 24, 25 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 74, and 75 years and over, for the calendar periods 1908-10, 1911-20, 1921-30, 1931-40, and 1941-5.

Mortality attributed to cancer of the breast among women aged 25 to 34 years remained fairly constant over the 37 years reviewed. At age 35 years and over, however, mortality increased. It is concluded that these trends represent a real increase in mortality due to cancer of the breast, because (a) diagnosis of patients who

subsequently died is not likely to have caused undue difficulty, and (b) mortality due to "presumed cancer of the breast" also increased in the same period among women of the same ages. It is suggested that in the past some deaths due to cancer of the breast may have been recorded under such vague designations as cancer of the neck, axilla, chest, heart, or lymph nodes, thereby resulting in an understatement of the early mortality rates of true breast cancer. The author combines deaths attributed to cancer of these sites with those attributed to breast cancer in order to obtain mortality rates for "presumed cancer of the breast".

Mortality attributed to cancer of the uterus declined between 1908 and 1945 at all ages under 65 years; it remained stationary in the age group 65 to 74 years and increased slightly at age 75 years and over. The decline in the rate at ages under 65 was relatively greater at the younger ages.

Mortality attributed to cancer of the ovaries, vagina, and vulva is tabulated for the same age groups for two calendar periods, 1908-30 and 1931-45. Deaths from cancer of these sites were considerably less numerous than those from cancer of the uterus, but a striking feature of the table is the consistent increase in mortality attributed to cancer of the ovaries between the two calendar periods. This increase became relatively greater as age advanced.

Finally, the author tabulates the number of deaths from cancer of the breast, uterus, other female genital organs, and all other sites combined, for each age group of women in three separate conjugal groups in the years 1931-40. The conjugal groups were: (a) "never married"; (b) "married and had children"; and (c) "married and did not have children". This information was not available for all the recorded deaths, and those which could not be so classified are omitted from the analysis. [The proportion of omissions to the total is not stated, but the number is said to be small.] In order to make a comparison between the three conjugal groups the author has calculated for each site the number of deaths to be expected in each age and conjugal group on the hypothesis that the proportion of deaths in each age and conjugal group is the same as the corresponding proportion for all forms of cancer combined. The differences between observation and expectation suggest that cancer of the breast was relatively more common among unmarried than among married women, whereas the reverse was true of cancer of the uterus.

E. A. Cheeseman

1745. **Some Suicide Statistics**

D. SWINSCOW. *British Medical Journal* [Brit. med. J.] 1, 1417-1423, June 23, 1951. 6 figs., 12 refs.

Death rates from suicide in England and Wales are examined for men and women separately in age groups: under 25 years, 25 to 44, 45 to 64, and over 65. Between 1861 and 1911 the rates for men showed a steady increase in each age group with, in each decade, the maximum rate falling in the 45 to 64-year group. Between 1911 and 1921 there was an abrupt decline at each age. In women the highest rate has been at ages 45 to 64, but otherwise the trend of their suicide rate between 1861 and 1921 was very similar to that shown by men. Since 1921 some new features have appeared. The death rates of men at 45 and above rose irregularly to a peak in 1932 and then fell steeply until 1942-3, broken by a slight peak in 1938. Since then the rates have risen continuously, though they still remain substantially below the pre-war values. At ages under 45 there has been a declining incidence since 1932, and there is no such post-war upward movement as is shown by the older age groups. With older women, 45 years and above, the curves show a rise up to about the year 1938 and then, after a sudden decline for a few years, a sharp rise between 1944 and 1949. At ages under 45 there has been little change since 1940.

These changes in the incidence of suicide since 1923 are, in men, closely associated with the prevailing level of employment; with women this association is much slighter, and it seems that unemployment, or the social conditions of which it is a feature, have some influence on the incidence of suicide among men, but none of significance on that among women. Examination of the age distribution shows that in the last 50 years suicide has increasingly become a disorder of elderly people. The highest incidence is found, in England and Wales, from spring until midsummer, and some statistics are given to show a converse seasonal distribution in Australia.

A. Bradford Hill

1746. **The Incidence of Dental Caries among Adults and Young Children in Three High- and Three Low-fluorine Areas in England**

J. R. FORREST, G. J. PARFITT, and E. R. BRANSBY. *Monthly Bulletin of the Ministry of Health, etc.* [Mon. Bull. Min. Hlth] 10, 104-107, May, 1951.

Experience in many parts of the world has shown a low incidence of dental caries in areas where the drinking-water has a high fluorine content. With a concentration above 1.5 parts per million (p.p.m.), mottling of the teeth, the first sign of fluorosis, becomes increasingly apparent; and with higher concentrations other changes, including toxic symptoms, appear. With a concentration of 1.0 to 1.2 p.p.m. there is a considerable reduction in the incidence of caries and no appreciable mottling.

The authors of this paper have carried out, in selected areas of England, an interesting survey which tends to confirm the above experience. Six areas were chosen, in 3 of which the water has a high fluorine content (from 0.7 to 2.0 p.p.m.) and in the other 3 a low content (from 0.0 to 0.5 p.p.m.). Each of the low-fluorine areas

resembled its high-fluorine counterpart except as regards the water supply, so that other factors were comparable.

Mothers attending antenatal and welfare centres and children attending nurseries and infant welfare centres were studied. The amount of caries present was assessed by indicating the number of decayed, missing, or filled teeth. Precautions were taken to eliminate personal factors, and the standard of dental examination was identical in all groups. In all, 268 adults and 434 children in the 3 high-fluorine areas, and 296 adults and 356 children in the 3 low-fluorine areas were examined. The children in each case were between 2 and 5 years old.

Among the mothers it was found that in the high-fluorine areas the incidence of caries was lower in every age group; there was apparently a delay of 10 years in the onset of caries, a smaller proportion of the teeth were actually missing, and the caries was less severe in the teeth present. Among the children it was found that in the high-fluorine areas a reduction in the incidence of dental caries was already apparent at 2 to 3 years of age (the reduction being less in the older children), and the proportion of children free from caries was greater.

[This investigation, which has obviously been carried out with great care, is important in that it provides confirmation of observations made by other workers, and that it indicates a cause of dental decay which is susceptible of prevention. It also points to the way in which public health investigations can be followed up by large-scale prevention.]

A. Trevor Jones

1747. **Ten Years of Diphtheria Immunisation**

D. THOMPSON. *Monthly Bulletin of the Ministry of Health, etc.* [Mon. Bull. Min. Hlth] 10, 132-136, June, 1951. 4 refs.

The author reports the results of the campaign for the immunization of children against diphtheria during the last 10 years. While in the preceding 10 years the average number of cases of diphtheria notified was 60,000 and that of deaths 3,115, and in 1941 there were 50,797 cases with 2,641 deaths, in 1950 the number of cases notified was 980 and the number of deaths 49. In 1949 the case-fatality rate for non-immunized children under 5 years of age in the whole country was 11.3%, and for immunized children 2.3%; for the age group 5 to 15 the figures were 3.8% and 0.33% respectively. The attack rates per 100,000 of the child population under 15 years of age in the whole country for 1949 made evident the immense value of immunization. The figure for immunized children aged 0 to 5 years was 6.8 and for children aged 5 to 15 years 7.0, while the rates for the non-immunized were 18.8 and 37.1 respectively. A comparison of the notifications in the different age groups in the years 1944 and 1950 showed that the fall in incidence continued to be smaller in the youngest and oldest age groups.

Diphtheria is more prevalent in females than in males. This preponderance may probably be explained by the fact that mothers and elder sisters come, through nursing, into closer contact with sick children. During the last 10 years 9,148,005 children under 15 years of age were

immunized and 2,145,095 received reinforcing injections. Up to 1949, 66% of the child population was protected, compared with only 8 to 10% before the campaign began. In 1950 the number of primary immunizations and reinoculations declined, especially among the older children: compared with 1949, the percentage of children under 5 inoculated was 75.4, and only 70.7 for those aged 5 to 14. This decline was due to the fear during times of epidemic that inoculation might produce the paralytic form of poliomyelitis. Statistics showed, however, that only 58 cases of poliomyelitis developed among 517,436 inoculated children. The risk is small compared with that of a recrudescence of epidemics of diphtheria; therefore the author is of the opinion that the proportion of immunized children must be kept up to at least the 70% level to assure a satisfactory protection against diphtheria.

Franz Heimann

EPIDEMIOLOGY

1748. **The Relation of Prophylactic Inoculations to the Onset of Poliomyelitis: a Study of 620 Cases in the Victorian Epidemic of Poliomyelitis in 1949**
B. P. McCLOSKEY. *Medical Journal of Australia [Med. J. Aust.]* 1, 613-618, April 28, 1951. 2 refs.

The author, who has previously reported his early findings (*Lancet*, 1950, 1, 659), discusses the influence of injections of diphtheria toxoid and pertussis vaccine in determining the incidence of poliomyelitis among the inoculated. Of 675 notified cases 620 were investigated. This figure includes the 375 cases of poliomyelitis previously reported. A total of 53 patients had been inoculated with diphtheria toxoid alone or in combination with whooping-cough vaccine within 3 months before the onset of symptoms. The severity of paralysis was greater in patients who had received an injection of pertussis vaccine alone or combined with diphtheria toxoid than in those who had received diphtheria toxoid alone.

Franz Heimann

1749. **A Localized Outbreak of Tinea Capitis (*M. audouini*) in Northern Ireland**
J. M. BEARE and E. A. CHEESEMAM. *Archives of Disease in Childhood [Arch. Dis. Childh.]* 26, 149-157, April, 1951. 2 figs., 12 refs.

This is a useful clinical and statistical study of an epidemic of tinea capitis occurring during a period of 15 months and affecting as many as 368 children out of a population of some 3,000 under the age of 17 years. The organism responsible was *Microsporum audouini*, which was the only fungus grown from 280 cultures; in every case there was a typical green fluorescence under Wood's light.

There was a striking difference in the attack rate between the sexes—27.2% of the boys being infected compared with 7.2% of the girls. There was no apparent association between age and incidence of infection. Varying grades of inflammatory reaction were seen, from severe kerion (6 cases) to virtually no reaction at all, the most common being that usually described as "grey

baldness". Diagnostically, the most troublesome cases were those presenting either no abnormality or only slight scaling, and the authors stress the importance of dandruff as a clinical sign of infection; such patients may act as carriers of infection for long periods. Wood's light was particularly valuable in the detection of cases of this kind. In early infections fluorescence is brilliant green and in long-standing cases a dull blue colour, and in the latter the number of infected hairs in any one area was found to diminish, while their length increased—factors which facilitated the estimation of the duration of an infection in any particular patient.

Of the total of 368 infected children, 90 were not subjected to x-ray epilation, and of these all but 3 were regarded as having spontaneous cure (24%); this series, however, is not regarded as a representative sample of all the spontaneous cures which might have occurred in the epidemic if mass x-ray epilation had not been introduced. Reinfection was found in only one case.

Finally, the authors emphasize that to the clinician the most important sign of tinea capitis in a child is dandruff and not alopecia, and that consequently Wood's light is absolutely essential for the diagnosis of the condition.

E. W. Prosser Thomas

1750. **Epidemic Diarrhea in a School for Boys**

T. H. INGALLS and S. A. BRITTEN. *Journal of the American Medical Association [J. Amer. med. Ass.]* 146, 710-712, June 23, 1951. 3 figs., 15 refs.

This paper records the symptomatology and epidemiology of an explosive epidemic of diarrhoea and vomiting in a New England residential school for boys. The pattern of incidence appears to exclude a food infection, and this conclusion is supported by the failure to find the usual pathogens in stools and vomitus and the occurrence of secondary cases in contacts outside the immediate school environment. Although diarrhoea and vomiting were both sudden and severe, the illness rarely lasted more than 24 hours, and there were neither complications nor severe general disturbance. In all, 141 out of 193 boys were affected in a space of 10 days.

Reference is made to similar outbreaks reported in British and Danish literature. A virus aetiology is suggested and a plea is made for further investigation of these outbreaks, which may be similar to the more serious type that affects newborn infants.

T. A. A. Hunter

1751. **An Epidemic of Q Fever in Dielsdorf. (Q-Fieber-Epidemie in Dielsdorf)**

O. BAUMGARTNER. *Praxis [Praxis]* 40, 178-180, March 1, 1951. 1 ref.

Within 12 days 30 cases of Q fever occurred amongst employees in a factory where preventives against plant disease were being manufactured; all the patients had been in contact with sheep used for experimental purposes. Some of the sheep gave a positive complement-fixation reaction. The disease, which did not spread to the surrounding district or the local hospital, ran a benign course. The presence of pneumonia was revealed by physical examination in only 3 cases, though it was

always found on x-ray examination when this could be carried out. Meningism occurred in 2 cases, and in one case there were subsequent attacks of dizziness. The diagnosis was confirmed serologically.

O. Gsell [*Excerpta Medica*]

1752. **The Epidemiology of Toxoplasmosis. The Dog as a Source of Human Infection.** (Zur Epidemiologie der Toxoplasmose. Der Hund als Infektionsquelle des Menschen)

E. OTTEN, A. WESTPHAL, and E. KAJAHN. *Klinische Wochenschrift [Klin. Wschr.]* 29, 343-346, May 15, 1951. 11 refs.

From the Bernard Nocht Institute, Hamburg, the authors report an investigation into the possible significance of the dog in the transmission of toxoplasmosis to human beings.

From within the city of Hamburg 122 dogs were obtained and subjected to the Sabin-Feldman serum colour test. In 49 the reaction was positive. This relatively high number of positive reactions is attributed to the fact that many of the dogs so tested were presenting signs suggestive of the disease (neuritis, paralysis, fits, or diarrhoea). Latent infection was uncovered in only 5 instances, while anamnestic reactions were not obtained. On a basis of careful sampling the authors conclude that from 2 to 5% of the dog population of Hamburg is probably infected with toxoplasmosis.

When a positive result was obtained the authors, where possible, also tested the owner of the dog. Of 38 persons so tested 23 gave positive reactions; 5 dog owners tested within 8 days of the appearance of the disease in their animals (for the most part nervous symptoms) proved negative. Of the owners of 6 dogs with chronic nervous symptoms, only 2 gave a positive reaction; on the other hand, of 8 owners whose dogs' main symptoms were gastro-intestinal 6 gave a positive reaction, as did also 10 of the 11 owners of dogs with mixed symptoms.

Diarrhoea in dogs suffering from toxoplasmosis appears to be due to necrotic lesions in the rectum and the authors conclude that this form of the disease is most liable to bring about infection in human beings. They consider that their investigations leave no doubt as to the importance of the dog in spreading toxoplasmosis.

Joseph Ellison

INDUSTRIAL MEDICINE

1753. **Pulmonary Tuberculosis Mortality in the Printing and Shoemaking Trades: Historical Survey, 1881-1931** M. CAIRNS and A. STEWART. *British Journal of Social Medicine [Brit. J. soc. Med.]* 5, 73-82, April, 1951. 2 figs., 15 refs.

The authors show in their survey that the increase in tuberculosis mortality among shoemakers was due to the change from working at home to working in factories, which introduced the possibility of cross-infection at work. That this does occur was confirmed by mass radiography, which revealed a positive correlation

between the number of workers and the incidence of overt tuberculosis. Among printers the death rate from pulmonary tuberculosis was over twice that for all males of working age, but in the last 50 years has steadily declined. The death rate from all other causes remained low in both trades.

Franz Heimann

1754. **The Reaction of the Lungs to Different Kinds of Coal Dust.** (Реакция легких на разные виды угольной пыли)

V. A. RAVVIN and P. A. ENYAKOVA. *Архив Патологии [Ark. Patol.]* 13, 79-84, 1951. 3 figs., 8 refs.

Bituminous and anthracite coal dust was introduced intratracheally in two series of rabbits, and the ensuing histological changes were studied for a period of 1 year. The silicon content of the dust was estimated and was found to be insignificant in both cases. It was observed that introduction of anthracite dust caused more severe and lasting changes, including the formation of argyrophil fibres in the alveolar walls. The authors do not dispute the deleterious effect of silicon when it is inhaled with coal dust, but believe that the difference which they have observed between the effect of bituminous coal and that of anthracite owes something to the inherent pathogenic properties of the latter.

L. Crome

1755. **The Medical Prophylaxis of Silicosis.** (La profilassi medicamentosa della silicosi)

P. ZEGLIO. *Rassegna di Medicina Industriale [Rass. Med. industr.]* 20, 65-107, March-June, 1951. 19 figs., bibliography.

This paper is divided into two parts: in the first the literature relating to the prophylactic and therapeutic treatment of silicosis is reviewed; and in the second the author's experiments are described and recommendations for prophylaxis made.

In the experimental section the author describes the preparation of a 2% suspension of aluminium hydroxide in 1% sodium chloride by adding a 2% solution of sodium carbonate to an equal volume of 2% aluminium chloride. This suspension, which consists of particles of about 1 μ diameter, is used to demonstrate the reduction by alumina of the solubility of quartz and the effect of alumina in accelerating the aggregation and sedimentation of quartz suspended in water, saline, or serum diluted with saline. This suspension, which remains stable for some hours, is used in an apparatus [not fully described] for the production of a prophylactic aerosol.

To prove the innocuous character of the aerosol, 6 guinea-pigs were exposed for 30 minutes daily to an atmosphere containing about 300 mg. of aluminium per cubic metre. [This represents about 10 times the daily exposure proposed for the treatment of human subjects.] After a year the 6 animals appeared to be in excellent health; 2 were killed, and their lungs were found to be normal.

A second group of 6 adult guinea-pigs were exposed for 3 hours twice daily to an atmosphere containing quartz particles less than 20 μ in diameter. Of these animals 3 received daily a 15-minute exposure to the aluminium hydroxide aerosol. The powdered quartz

was dispersed by compressed air, a quantity being blown into the dusting chamber at hourly intervals. The concentration, as determined by thermal precipitator samples, varied between 200,000 and 10,000 particles per c.cm.

At the end of 10 months 2 of the animals receiving silica only were losing weight, showed accelerated respiration, and in one case refused food; the remainder appeared well. Two of each set of 3 were killed. Macroscopically, the lungs of the 2 pairs showed slight differences—the pair exposed only to silica showed more enlargement of the mediastinal and tracheal lymph nodes and their lungs were firmer to the touch. Chemical analysis of lung tissue revealed approximately twice as much silica in the lungs of those receiving silica only as in the others. This was confirmed by the appearance of sections under the polarizing microscope. Lung sections were stained with haematoxylin-eosin, and with van Gieson stain for connective tissue. Examination of sections showed invasion of the lung by fibrous tissue, and thickening of the alveolar walls leading to disappearance of the alveoli from large areas; occasional necrotic zones were seen in this dense tissue. No typical hyaline nodules were apparent. Under polarized light doubly-refracting particles were seen in the necrotic zones, in the perivascular lymphatics, and especially in giant cells in the neighbourhood of the alveolar ducts. The few remaining alveoli, the alveolar ducts, and the respiratory bronchioles were generally empty. The animals receiving aluminium hydroxide in addition showed changes similar to these, but much less advanced; numerous cellular elements were present in the alveoli and bronchioles, including dust-containing macrophages.

Inhalation of the aluminium hydroxide aerosol was well tolerated by 4 volunteers, who remained for 3 hours in a chamber containing about 60 mg. of alumina per cubic metre. In factories where there is a silicosis risk the following mixture is recommended for dispersion as aerosol in changing-rooms: aluminium hydroxide, 2%; sodium hyposulphite, 0.2%; sodium benzoate, 0.5%; sodium *para*-aminobenzoate, 0.3%; oil of bergamot, 0.1%; in water at pH 7.3 to 7.5. Workmen should be exposed for 10 to 15 minutes at the end of each shift.

[The absence of nodulation in both groups of animals and the smaller amount of silica in the animals receiving aluminium hydroxide are noteworthy and in marked contrast to the findings of others (for example, King, Wright, Ray, and Harrison, *Brit. J. industr. Med.*, 1950, 7, 27). As the author remarks, the experiments should be repeated with larger groups of animals.]

J. W. Roe

1756. Carcinogenic Hydrocarbons and Related Compounds in Processed Rubber

H. L. FALK, P. E. STEINER, S. GOLDFEIN, A. BRESLOW, and R. HYKES. *Cancer Research [Cancer Res.]* 11, 318-324, May, 1951. 15 figs.; 16 refs.

In experiments with rubber stoppers it was found that benzene extracts of the stoppers induced papillomata and carcinomata when painted on the skin of mice. These extracts and that from a motor-car tyre were shown to

contain aromatic hydrocarbons, one of which (3:4-benzpyrene) is a potent carcinogen and others of which are known to be weak carcinogens. The carcinogens are most probably introduced into the rubber during the processing, in which carbon black is used. This material is made by incomplete combustion of natural gas, oils, and tars and may be the source of the carcinogens. In the processed rubber the latter are present only in small amounts and are relatively inaccessible to contact exposure. No evidence exists that exposure to products containing carbon black constitutes a practical hazard. They may be harmless under ordinary conditions of exposure, but when some organic solvents are used, as under laboratory conditions, extraction is easy and there is then danger of accidental unrecognized contamination during experiments in cancer research.

I. A. Elson

1757. The Effect of BAL in the Prevention and Treatment of Experimental Skin Lesions due to Chromium Derivatives. (Sull'azione preventiva e terapeutica del B.A.L. nelle lesioni cutanee sperimentali da derivati del cromo)

G. FARRIS and U. SICCA. *Rassegna di Medicina Industriale [Rass. Med. industr.]* 20, 169-182, March-June, 1951. 7 figs., 26 refs.

For the purpose of studying the efficacy of BAL in the prevention and treatment of skin lesions due to exposure to chromium derivatives, ulcers were produced as follows: the skin was sterilized with Dakin's fluid and a small area scarified with a sterile needle; a drop of chromic acid solution (10%) was applied to the area and the place then covered with gauze. This was repeated daily for 3 days. After about 6 days a satisfactory ulcer had developed. Two ulcers were produced on the forearm of each of 3 volunteers, and to one of each pair an ointment containing 10% BAL was applied. This treatment did not sensibly accelerate healing.

A cream containing 10% BAL was next tested. One arm of each of 5 volunteers was scarified in 3 places and each site was subjected to one of the following procedures: (a) a drop of 10% chromic acid was applied; (b) a drop of 10% BAL cream followed by a drop of chromic acid, and the two mixed together; and (c) a drop of cream containing no BAL followed by a drop of chromic acid, and the two mixed. The arm was maintained in a horizontal position for 15 to 20 minutes, then dressed with sterile gauze. The excipient cream was in all cases a preparation of polyglycol. This treatment was repeated on 3 successive days. On the 7th day the responses in the 5 arms were found to be identical. At (a) was a typical ulcer 7 to 10 mm. in diameter; at (c) a small yet typical ulcer 2 to 3 mm. in diameter; and at (b) no specific lesion.

In a further experiment a barrier cream containing 15% BAL applied 3 to 4 times daily to the hands and forearms of 10 volunteers was found to produce no sign of irritation or other response in 4 to 5 days.

Their results have led the authors to propose the use of a barrier cream containing 5% BAL as a protection against chromium derivatives.

J. W. Roe

Genetics

1758. The Genetics of "Cystinuria"

C. E. DENT and H. HARRIS. *Annals of Eugenics [Ann. Eugen., Camb.]* 16, 60-87, July, 1951. 2 figs., 34 refs.

Chromatographic, clinical, and familial evidence indicates that an increased excretion of cystine in the urine may be due to several distinct conditions. From a study of the literature and of 11 propositi and their families the authors describe three types of genetically determined cystinuria:

(a) *Classical cystinuria*. Patients usually enjoy good health, but cystine stones occasionally form in the urinary tract. The urine always contains large quantities of cystine and lysine and usually of arginine. An identical condition is frequently found in close relatives. The possible mode of inheritance is discussed.

(b) *Fanconi syndrome*. This condition comprises unusually vitamin-D-resistant rickets (in children) or osteomalacia (in adults), chronic acidosis, hypophosphataemia, renal glycosuria, and a large excretion of numerous amino-acids. In one family 3 apparently healthy sibs were found in whom biochemical changes almost identical with those in the propositus were present.

(c) *Wilson's disease*. The neurological symptoms are sometimes associated with a large excretion of numerous amino-acids, including cystine.

The possibility is discussed that a larger body of familial data may reveal that a further genetical subdivision of biochemically indistinguishable types is necessary and that dominant and recessive types occur. In the case of Fanconi's syndrome, familial investigation may afford the opportunity to watch, and maybe treat prophylactically, clinically unaffected relatives of patients.

H. Kalmus

1759. The Familial Occurrence of Disseminated Sclerosis

R. T. C. PRATT. *Annals of Eugenics [Ann. Eugen., Camb.]* 16, 45-59, July, 1951. 1 fig., 24 refs.

In this investigation from the Middlesex Hospital Medical School, London, the author compared the corrected incidence of disseminated sclerosis in the sibs and parents of 186 unselected patients with the estimated incidence (of the order of 1 in 2,000) in a control population. In the former group he found the rate to be about 10 times this value. Among the parents of the patients first-cousin marriages were significantly more frequent than in the general population, indicating that a few cases of the disease may be caused by rare recessive genes. This is in agreement with the literature. If two sibs are suffering from disseminated sclerosis they are more likely to be like-sexed than unlike-sexed. There was a deficiency of first- and second-born children in the material studied, and the age of the mothers at the time of the patients' birth was significantly raised. According

to the literature the incidence among twin sibs, whether monozygotic or dizygotic, of patients suffering from disseminated sclerosis seems to be raised. The author concludes that with the material at present available the precise mode of inheritance of disseminated sclerosis cannot be determined.

H. Kalmus

1760. The Familial Incidence of Disseminated Sclerosis and its Significance

R. T. C. PRATT, N. D. COMPTON, and D. MCALPINE. *Brain [Brain]* 74, 191-232, 1951. 2 figs., bibliography.

Detailed family histories were obtained from 310 patients suffering from disseminated sclerosis. In the first group of 142 patients inquiries were made concerning only parents and sibs, and at least one affected relative was found in 8 instances. In the second group of 168 consecutive patients seen during a period of 18 months, more extensive inquiries were made, and 12 instances were found of more than one relative being affected.

It was estimated that the incidence of the disease among the living brothers and sisters of the patients was about 1 in 100, and among the living parents about 1 in 150. The incidence of the disease in the general population was estimated as being of the order of 1 in 2,000, and there seemed little doubt, therefore, that the familial incidence was significantly higher than would have been expected on a chance basis. This familial incidence might be due to either a "common environment" or the influence of hereditary factors. The latter was considered the more likely because of the rarity of the disease in unrelated associates or in husband and wife, and also because of the occasional appearance of the condition in close relatives who had not met at any time during their lives.

A more detailed genetical analysis of the findings is presented elsewhere (see Abstract 1759).

Harry Harris

1761. Sickle-cell Trait in Yemenite Jews

F. DREYFUS and M. BENYESCH. *Nature [Nature, Lond.]* 167, 950, June 9, 1951. 1 ref.

Of 105 unselected children of Yemenite Jews, recent immigrants to Palestine, 7 were found to have the sickle-cell trait: the families of 6 of these were further studied and 5 more cases detected.

The authors admit the uncertain ancestry of the Yemenite Jews, but point out that they do not resemble negroes and that heavy admixture with negro blood is improbable. They are the only Jews in whom the trait is known to occur, and it is suggested that they may form a new focus, independent of that in Africa. [This conclusion is questionable, because negro slaves have been imported into Arabia since time immemorial.]

G. Discombe

Anatomy and Cytology

1762. Observations on the Pre-natal Development of the Intervertebral Disc in Man

A. PEACOCK. *Journal of Anatomy [J. Anat., Lond.]* **85**, 260-274, July, 1951. 22 figs., 47 refs.

In a study of the pre-natal development of the intervertebral disk a series of 38 human embryos and foetuses, ranging from 3-mm. embryos to full-term foetuses, were examined. The author found that the disk develops from the densely aggregated mesoderm on both sides of the fissure of von Ebner, and thus receives contributions from both cranial and caudal half-sclerotomes. Development proceeds from the notochord, the peri-notochordal tissue (which forms a specialized embryonic cartilage which later gives rise to the fibro-cartilaginous component of the disk), and the dense mesoderm previously noted which forms the annulus fibrosus. In the thoracic region the hypochordal bow can be identified taking part in the formation of the ventral part of the disk. The annulus fibrosus develops rapidly, and its fibrous bands, passing both concentrically and obliquely from one vertebra to the next, are complete in early foetal life. The notochord shows a progressive, intervertebral expansion as growth proceeds, and at birth forms a considerable proportion of the area of the whole disk. It was found in this series that small vessels run in the peripheral lamellae of the annulus fibrosus, but the nucleus pulposus remains avascular during foetal life.

Peter Ring

1763. The Structure of the Glomerular Capillaries as seen with the Electron Microscope. (La structure des capillaires glomérulaires vue au microscope électronique)

C. OBERLING, A. GAUTIER, and W. BERNHARD. *Presse Médicale [Pr. méd.]* **59**, 938-940, July 4, 1951. 12 figs., 11 refs.

For the purpose of carrying out an electron-microscopic study of the structure of the glomerular capillaries, kidney tissue was fixed in 1 or 2% osmic acid or in Champy's fluid—by perfusion in the case of rats and mice, and by immersing thin slices in the fixative when working with tissue from human subjects. Tissues were embedded in "esterwax" and sections were cut about 2 μ thick with a microtome of the Cambridge rocker type. The authors give the following description of their findings.

In the centre of each glomerulus there is connective tissue—the mesangium of Zimmermann—to which the capillaries are attached. Their extremely thin walls, formed by the flattened epithelial cells, are supported by a trellis-like structure presenting the appearance of honeycomb. The basement membrane is smooth on the inside, but externally is thrown up in a complicated series of folds. The epithelial glomerular cells which cover the basement membrane externally have a similar compli-

cated system of folds on their internal membrane. Also, intricate ramifications formed by adjacent epithelial cells interdigitate to produce maze-like patterns of a "complexity defying all description". This structure is regarded as serving a double function: it affords mechanical support for the walls of the capillaries, and by providing an extensive system of narrow intercellular spaces reinforces the process of glomerular filtration by capillary attraction.

R. J. Ludford

1764. Morphological Observations on the Mechanism of Multiplication and Nuclear Division in the Giant Cells of the Bone-marrow. (Morphologische Beobachtungen über den Vermehrungs- und Kernteilungsmechanismus der Knochenmarksriesenzellen)

H. WEICKER and H. G. NÖLLER. *Klinische Wochenschrift [Klin. Wschr.]* **29**, 184-190, March 1, 1951. 26 figs., 11 refs.

This study from the Paediatric Clinic of Heidelberg University is based on a morphological survey of 10,000 megakaryocytes observed in bone-marrow smears from healthy children and from children with idiopathic thrombocytopenic purpura and with typhoid fever. The nuclear and cytoplasmic details of the cells were noted; the 50 mitotic figures found were particularly carefully investigated.

No evidence has been discovered for the theories of amitotic division and of nuclear conglomeration in the development of mature megakaryocytes. Most mitoses are found at the promegakaryocyte stage, very few in mature megakaryocytes. Prophases are very rarely seen; metaphases are most numerous. In early cells, which are most monophoid, the angle of the chromosomes is usually 80 to 110 degrees, their length usually up to 10 μ , and they number 35 to 100 in any one cell. Pseudopodia are not uncommon, but amoeboid movements of megakaryocytes have not been observed. Cells of the same generation, even if found near each other, may differ in the degree of maturation. In smears, more than half the megakaryocytes in mitosis measure 40 to 45 μ in diameter and show polyploid sets of chromosomes. Sometimes they have 100 to 600 chromosomes, often arranged in 3 to 8 areas, leading to multipolar mitoses. On the other hand, lobation of the nucleus is also often already seen in megakaryoblasts and may not always be due to mitosis. Nucleoli do not appear to be altered by mitosis in the cells, but it is not certain whether their function is the same as that of nucleoli in other marrow cells. The relationship between mitotic polar arrangement and lobation or segmentation and also platelet formation is not established. There is no difference between the behaviour of normal megakaryocytes and those of idiopathic thrombocytopenic purpura.

E. Neumark

Physiology and Biochemistry

1765. The Effect of Posture on Diaphragmatic Movement and Vital Capacity in Normal Subjects, with a Note on Spirometry as an Aid in Determining Radiological Chest Volumes

O. L. WADE and J. C. GILSON. *Thorax [Thorax]* 6, 103-126, June, 1951. 13 figs., bibliography.

With the aid of a mechanical device for tracking the fluoroscopic shadow of the movements of the diaphragm and a spirometer simultaneous records of diaphragmatic movement and respiration were made. Twelve normal subjects were examined in a variety of postures, and it was found that during quiet breathing the movement of both diaphragms was about 1.5 cm., and during deep respiration 6 or 7 cm. A close relationship was found between the volume of reserve air and the extent of movement of the diaphragm above its resting level. When the subject is lying on his side, the pattern of movement of the lower diaphragm is similar to that of both domes when the subject is lying supine or tilted 45 degrees head down; in such a position the lower lung appears to be relatively compressed.

Kenneth Marsh

1766. Vasomotor, Cellular and Functional Changes Produced in Kidney by Brain Stimulation

E. C. HOFF, J. F. KELL, N. HASTINGS, D. M. SHOLES, and E. H. GRAY. *Journal of Neurophysiology [J. Neurophysiol.]* 14, 317-332, July, 1951. 8 figs., 12 refs.

Electrical stimulation of the anterior sigmoid gyri in curarized cats produced a transient rise in arterial blood pressure; the renal cortex became ischaemic, as observed under white light or under ultraviolet illumination following intravenous injection of fluorescein. The cortical ischaemia of the kidney was also shown by intra-arterial injection of indian ink during the hypertensive effect. The ischaemic changes in the kidney did not occur when renal denervation had previously been carried out. Fatty degeneration of the kidney tubules and fragmentation of the tubule-cell nuclei occurred. In survival experiments with repeated stimulation of the cortex through the unopened skull over a period of 1 to 6 weeks histological examination revealed lower-nephron nephrosis. It is assumed that these changes are due to tissue anoxia and alterations in capillary permeability in response to repeated arteriolar vasoconstriction.

A. Schweitzer

1767. Expulsion of Respiratory Gases from Lungs of Human Subjects during Rapid Decompression

F. G. HALL and K. D. HALL. *Journal of Applied Physiology [J. appl. Physiol.]* 4, 1-6, July, 1951. 2 figs., 6 refs.

The pattern of gas expulsion from the lungs of human subjects during explosive decompression to 225 mm. Hg (equivalent to 30,000 feet or 9,000 m.) was studied by recording with a differential optical manometer the

pressures developed on each side of a fine wire-gauze barrier inserted into the expiratory valve of a mask worn by the subject. From the records the volume of gas expelled and the maximum rate of flow were calculated. The volume of gas expelled was approximately that expected on theoretical grounds. Very little resistance appeared to be offered to the flow of expanding gases from the lungs. Oxygen and carbon dioxide percentages in the final portion of expelled air were higher than in alveolar air at the initial pressure from which decompression occurred. No adverse effects were observed to result from repeated decompression.

R. A. Gregory

1768. Pigments of Blood and Bile

C. RIMINGTON. *Lancet [Lancet]* 2, 551-556, Sept. 29, 1951. 10 figs., 39 refs.

CIRCULATORY SYSTEM

1769. Comparison of Intracardiac and Intravascular Temperatures with Rectal Temperatures in Man

L. W. EICHNA, A. R. BERGER, B. RADER, and W. H. BECKER. *Journal of Clinical Investigation [J. clin. Invest.]* 30, 353-359, April, 1951. 4 figs., 7 refs.

Temperature measurements were made within the heart and various veins of 24 afebrile subjects by means of thermocouples introduced through cardiac catheters. There was a small but consistent gradient of increasing temperature in the larger veins as they approached the heart, the gradient being steeper in the thorax than in the abdomen, where it was sometimes absent. Sharp increases in temperature were noted in veins draining the liver and the brain. Rectal temperature was higher than intracardiac or vascular temperature. Equal values were obtained from the right heart and the pulmonary and femoral arteries.

A. Schweitzer

1770. Radioactive Sodium (Na^{24}) in the Measurement of Local Blood Flow

R. SEMPLE, L. McDONALD, and R. P. EKINS. *American Heart Journal [Amer. Heart J.]* 41, 803-809, June, 1951. 2 figs., 10 refs.

The rate of clearance of ^{24}Na from the gastrocnemius muscle was observed 42 times in 34 subjects; 18 observations were made on 11 normal subjects between 21 and 32 years old; 10 observations on 10 normal subjects between 45 and 70 years old; and 14 observations on 13 subjects over 45 years with occlusive arterial disease and intermittent claudication. A solution of 0.5 ml. of isotonic sodium chloride containing 5 $\mu\text{c.}$ of ^{24}Na was injected 2 cm. deep in the midline of the calf 12 cm. below the bend of the knee. All subjects had rested

for 40 minutes and lay comfortably prone. Counts were made with a Geiger-Müller counter above the site of the injection at 1-minute intervals for 10 minutes and at rest after walking; results were expressed as the "half-dispersal time". At rest a wide scatter was found, the results in the arteriosclerotic subjects falling within the normal range. The ratio of the half-dispersal time before exercise to that after exercise showed a similar variability, the readings in the arteriosclerotic cases again falling within the normal range.

The authors conclude that this method may not justifiably be used to assess the effects of therapy in peripheral vascular disease.

D. Verel

1771. Consistency of Clearance of Radioactive Sodium from Human Muscle

L. H. WISHAM, R. S. YALOW, and A. J. FREUND. *American Heart Journal* [Amer. Heart J.] **41**, 810-818, June, 1951. 4 figs., 3 refs.

The half-dispersal time of ^{24}Na was measured in the gastrocnemius and biceps in normal subjects. In each of 10 subjects 5 injections of 1 to 6 μC . ^{24}Na in 0.05 to 0.1 ml. isotonic sodium chloride were made in the belly of the gastrocnemius, 1½ in. (3.74 cm.) deep. The time between injections ranged from 1 day to several months. In each of 6 subjects 5 injections were made 1 in. (2.5 cm.) deep in the biceps, and the muscle was exercised by raising a 5-lb. (2.25-kg.) or 15-lb. (6.75 kg.) weight by flexion of the elbow from 180 degrees. In each subject three observations were made to determine the range of the clearance rate for each individual. This was obtained from the formula: range = average \pm 2 times S.D., and it was usually less than $\pm 20\%$ of the average clearance rate for any one individual. Two more observations were then made from 1 week to 2 months after the range had been established. Only one of these observations fell significantly outside the predicted range, and 2 were just outside the predicted range, for the individual concerned.

Moderate exercise of the biceps increased the clearance rate, and the increase after approximately equal amounts of work fell within 25% of the average for that individual. After fatiguing exercise the limits were $\pm 20\%$ of average. Clearance rates from the gastrocnemius while the subject stood did not differ significantly from those while the subject was prone. The authors suggest that the method may be of use in determining gross changes in blood flow.

[In this paper the terms "clearance rate of radioactive sodium" and the "effective blood flow" are used synonymously. The term "effective blood flow" is not defined.]

D. Verel

1772. A Hormonal Neurogenic Vasopressor Mechanism

R. D. TAYLOR, I. H. PAGE, and A. C. CORCORAN. *Archives of Internal Medicine* [Arch. intern. Med.] **88**, 1-8, July, 1951. 2 figs., 21 refs.

In acute experiments the vascular system of the central nervous system of one dog (A) was isolated from that of the rest of the body and connected up with that of a donor dog (B). When the central end of the vagus of

dog A was stimulated for 2 to 6 minutes the arterial pressure of dog B showed a gradual rise which slowly disappeared when stimulation in dog A ceased. In anaesthetized dogs in which the spinal cord had been destroyed below C6 stimulation of the central end of the vagus caused a similar slow rise in blood pressure. Injection of tetraethylammonium chloride greatly augmented the response. It was not depressed by administration of piperoxan hydrochloride (which reverses the action of adrenaline and depresses that of noradrenaline) or tolazoline (which reverses the effect of both adrenaline and noradrenaline). "C-5968" (1-hydrazinophthalazine) abolished the pressor response to vagal stimulation. This drug only slightly impaired the response to renin and to angiotonin, but partially reversed the response to serotonin.

It is suggested that the pressor substance liberated on vagal stimulation is similar to serotonin. In an addendum it is stated that the pressor substance was liberated in similar experiments on stimulation of the central end of the sciatic nerve.

R. A. Gregory

1773. Ventricular Ectopic Rhythms and Ventricular Fibrillation following Cardiac Sympathectomy and Coronary Occlusion

A. S. HARRIS, A. ESTANDIA, and R. F. TILLOTSON. *American Journal of Physiology* [Amer. J. Physiol.] **165**, 505-512, June, 1951. 2 figs., 11 refs.

Upper thoracic sympathectomy preceding occlusion of the anterior descending artery of the dog reduces, but does not completely prevent, ectopic ventricular fibrillation during the first 10 minutes (first phase) of occlusion. During the next 4½ to 8 hours (second phase) ectopic ventricular activity has been observed only during awakening following operations in which soluble thiopentone has been used. This ectopic activity was not observed in cases where upper thoracic sympathectomy preceded coronary occlusion. Previous sympathectomy does not change the time of onset of the third-phase ectopic activity (4½ to 8 hours), but it does reduce its duration.

The authors conclude that there is a multitude of excitatory factors that produce ectopic impulses during all phases.

Kenneth Marsh

1774. Experimental Pulmonary Arteriovenous Fistula

T. TAKARO, H. E. ESSEX, and H. B. BURCHELL. *American Journal of Physiology* [Amer. J. Physiol.] **165**, 513-519, June, 1951. 2 figs., 16 refs.

Experimental pulmonary arterio-venous fistulae in dogs were produced by end-to-end anastomosis of the artery and major vein supplying removed lobes. In acute experiments the mean pulmonary arterial pressure decreased, the mean carotid arterial pressure increased, and arterial oxygen saturation decreased when such a fistula was opened. In survival studies 4 of 16 animals in which the procedure was carried out survived for weeks or even months with arterial oxygen saturation ranging from 66 to 90%. In 2 animals with patent fistulae chronic hypoxaemia with secondary polycythaemia, hypervolaemia, and raised haematocrit

readings were found. An inverse relationship between arterial oxygen saturation and oxygen capacity was found in these 2 animals for periods up to 65 weeks.

Kenneth Marsh

1775. The Role of the Liver in the Process of Coagulation of the Blood. (De l'intervention du foie dans les phénomènes de la coagulation du sang)
P. NOLF and M. ADANT. *Sang [Sang]* **22**, 257-278, 1951. 17 refs.

This paper reports a study of changes in coagulation following total hepatectomy in dogs after anastomosis between the heart and the portal vein or between the heart and the vena cava below the liver. Variations were found in the anticoagulation power of the plasma, and these were still being investigated. The thrombozyme concentration was decreased, but less so than thrombogen. The thromboplastin (A-fibrinogen) level increased progressively after injection of peptone into hepatectomized dogs. This is regarded as proof of its extrahepatic origin.

A. Piney

1776. Experiments on a New Clotting Factor (Factor VII). [In English]
F. KOLLER, A. LOELIGER, and F. DUCKERT. *Acta Haematologica [Acta haemat., Basel]* **6**, 1-18, July, 1951. 7 figs., 46 refs.

The investigation described in this paper is based on the finding that with Owren's one-stage prothrombin technique no great loss of prothrombin potency in serum occurred during days or even weeks, whereas with Quick's one-stage or with a two-stage technique, serum values rapidly fall to low levels. This discrepancy suggested the presence of an accelerator in the serum. Furthermore, in Owren's method Seitz-filtered ox plasma is used, and Seitz-filtered human plasma does not give high serum prothrombin values. The present authors concluded that the factor present in the ox plasma might prove to be prothrombin.

Their experiments were designed to obtain evidence of the presence of an accelerator in serum free from other clotting factors. A method is described for its preparation from human serum and also for the preparation of ox plasma free from accelerator. The evidence obtained supports the view that the ox-plasma factor is prothrombin, and that there is a substance (called Factor VII by the authors) present in the preparation made from human serum which influences the rate but not the amount of thrombin formation. This substance remains almost unchanged during the coagulation process.

A. Brown

1777. A New Human Blood Factor of Rare Incidence in the General Population
P. LEVINE, A. H. STOCK, A. B. KUHMICHEL, and N. BRONIKOVSKY. *Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol., N. Y.]* **77**, 402-403, July, 1951. 7 refs.

A new blood factor, Mi^a, demonstrable with the aid of an immune isoantibody prepared for hemolytic disease of the newborn is briefly described. Its hereditary

nature is indicated by its presence in 4 out of 10 individuals in three generations of a particular family, in contrast to its absence in 425 random bloods.—[Authors' summary.]

DIGESTION AND METABOLISM

1778. The Significance of Bile to Proteolysis
L. K. CHRISTENSEN. *Gastroenterology [Gastroenterology]* **18**, 235-243, June, 1951. 3 figs., 8 refs.

In this paper the proteolysis of native globular proteins is discussed. Thrice-recrystallized β -lactoglobulin and egg albumen were hydrolysed with either crystalline pepsin (0.092%) or trypsin (0.0041%) both in the presence and in the absence of bile salts (0.025% sodium taurocholate or 0.085% sodium desoxycholate). Samples were withdrawn at intervals and examined for free carboxyl groups and optical rotation. Since the bile salts greatly increased the rate of hydrolysis, the possibility that bile salts assist in protein digestion is suggested. The resistance of the protein of the gastric and intestinal mucous membrane to proteolysis by its own secretions is discussed. The need for selecting well-defined, fully denatured substrates for measuring proteolysis in gastrointestinal juice and other biological materials is emphasized.

J. E. Page

1779. The Effect of Insulin on the Absorption of Glucose from the Intestine. (Acción de la insulina sobre la absorción intestinal de glucosa)
A. SOLS. *Revista Española de Fisiología [Rev. esp. Fisiol.]* **7**, 1-5, 1951. 1 fig., 19 refs.

It is known that the most important endocrines exert some influence on the selective absorption of sugar, but only thyroxine acts directly in this manner (Althausen). It has also been proved that insulin increases the absorption of glucose from the intestine of diabetic rats. The author, using a method described in a previous paper (*Rev. esp. Fisiol.*, 1947, 3, 207), found that the intravenous injection of insulin in normal rats provoked a 10% increase in the absorption of glucose from the intestine. He is of the opinion that this increased absorption may be connected with change in the local enzyme systems, especially in the hexokinase complex.

In diabetic animals glucose is not fixed in the liver and muscles because the activity of hexokinase is inhibited. Insulin can reactivate hexokinase in hyophysectomized animals; thus insulin may well act on hexokinase in the diabetic intestine and cause an increased absorption of sugar. It is also very likely that the first stage in this absorption takes place at a very superficial level of the intestinal epithelium and varies with the pH. Insulin taken by mouth does not increase the absorption of glucose.

Paul B. Woolley

1780. Effect of Vitamin B₁₂ on the Synthesis of Protein and Nucleic Acids in the Liver
M. R. SAHASRABUDHE and M. V. LAKSHMINARAYAN RAO. *Nature [Nature, Lond.]* **168**, 605-606, Oct. 6, 1951. 6 refs.

1781. Tolerance of Human Beings to Intravenous Infusions of Fifteen per cent Invert Sugar

J. J. WEINSTEIN. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 38, 70-77, July, 1951. 4 figs., 7 refs.

Invert sugar is produced by the hydrolysis of sucrose and consists of equal moles of D-glucose and D-fructose. The author has previously reported on the tolerance of human beings to the intravenous infusion of 50 g. and 100 g. of invert sugar. In the present study a single infusion of 150 g. of invert sugar in 1 litre of water, at a controlled rate of 2.5 g. per kg. of body weight per hour, was given to 21 adult surgical patients considered as being normal subjects. Breakfast was eaten at approximately 2 hours before the infusion; urine was collected by voluntary voiding before the test and immediately after, and at 1, 2, and 3 hours after the infusion; blood samples were taken from the opposite arm before the infusion, when 500 ml. and 1,000 ml. had been given, and at 1, 2, and 3 hours after the infusion. The average time taken over the infusion was 89 minutes; no food was allowed during the 4½-hour period of study, but 250 ml. of water was given at the beginning and 250 ml. at the end of the infusion, making a total fluid intake of 1,500 ml.

The urinary excretion showed an average loss of 5.5 g., or 3.6%, of the 150 g. of sugar injected, showing that 96.4% was retained and utilized; the older patients in the group showed as good a tolerance as the younger patients. Fructose constituted only 13% of the total reducing sugar recovered from the urine and only 12.3% of the total circulating reducing substance in the blood at the end of the infusion. These findings indicate that the fructose of the invert sugar was more rapidly removed from the blood, was retained in greater quantity, and was more rapidly assimilated than was the glucose. The haematocrit readings showed a fall which represented an average haemodilution of 10% or an increase of 450 to 500 ml. in blood volume. No adverse cardiac or pulmonary effects were observed clinically and there was no undue diuresis.

It is concluded that "invert sugar can be given rapidly by vein in large quantities, and in moderate amounts of fluid, with the assurance of a minimal loss in the urine and a ready retention by the body for utilization".

Joseph Parness

1782. The Morphologic Distribution of Intravenously Injected Fatty Chyle and Artificial Fat Emulsion in Rats and Dogs

R. G. MURRAY and S. FREEMAN. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 38, 56-69, July, 1951.

In this paper the term "chyle" refers to chyle previously collected from the thoracic duct of dogs which had been fed by stomach-tube with 4 g. of olive oil per kg. of body weight 3 to 5 hours before the removal of the chyle; the term "emulsion" refers to an olive-oil emulsion which was prepared so that it had a uniform particle size of about 1 µg. Chyle or emulsion, in amounts containing 0.6 to 1.2 g. of fat per kg. of body

weight, was rapidly injected intravenously into rats and dogs; the animals were killed at intervals of from 10 minutes to 24 hours after injection, and the organs were examined for distribution of fat by the staining of frozen sections with "oil red O"; biopsy of liver and spleen was carried out at an interval before the infusion, and serial biopsy specimens of liver tissue were also taken from 4 dogs up to 24 hours after injection.

In the spleen, the fat of the emulsion always appeared at 10 minutes after the injection in large amounts in the marginal zone of the red pulp, but the fat of chyle was never concentrated there. In the liver of dogs (and, less consistently, in that of rats) the fat of emulsion was concentrated in the Kupffer cells at 10 minutes after the injection, whereas at the same interval chyle fat appeared in the parenchymatous cells but was never concentrated in the Kupffer cells. The lung capillaries of rats were packed with fat at 10 minutes after the injection of emulsion, but chyle fat was never concentrated in the lung. Fat did not appear in significant quantity outside blood vessels—in cervical lymph nodes, kidney, heart, thymus, stomach, duodenum, or ileum—after injections of either chyle or emulsion.

The results in all organs, taken together, appear to indicate that the emulsion fat, while appearing almost as finely divided as the chyle, is not dealt with by the body in exactly the same way, but is treated much like a foreign substance. Thus it would appear that the fat of chyle enters the liver cells direct, whereas the fat of emulsion enters the liver cells somewhat more slowly by way of the Kupffer cells. In the same study, when 3 ml. of olive oil was given to rats by stomach-tube, fat could not be identified in spleen, liver, or lung.

Joseph Parness

1783. The Metabolism of Histamine

J. H. GADDUM. *British Medical Journal [Brit. med. J.]* 2, 987-991, Oct. 27, 1951. 1 fig., 40 refs.

ENDOCRINE SYSTEM

1784. Radioactive Decay and Metabolic Loss of Iodine from Normal Thyroid

F. J. BURNS, W. A. FISH, J. W. HACKETT, and F. C. HICKEY. *Journal of Applied Physiology [J. appl. Physiol.]* 4, 15-20, July, 1951. 4 figs., 7 refs.

In a study of the metabolic loss of iodine from thyroid tissue 2 adults with normal thyroid function were each given 100 µc. of radioactive iodine to which 100 µg. of potassium iodide had been added as carrier. The thyroid radio-iodine content was then measured *in vivo* over a period of 50 days. After correcting for the physical decay of the radio-iodine, the extrapolated metabolic half-lives of ¹³¹I in the thyroids were found to be 94 and 115 days respectively.

G. Ansell

1785. Evidence for a Non-thyroxine Thyroid Factor which Affects Gastric Function

R. N. WATMAN and E. S. NASSET. *American Journal of Physiology [Amer. J. Physiol.]* 166, 131-136, July 1, 1951. 8 refs.

1786. The Parathyroid Control of Serum Calcium Independent of Renal Mediation

G. S. STEWART and H. F. BOWEN. *Endocrinology [Endocrinology]* **48**, 568-575, May, 1951. 4 figs., 16 refs.

The degree of control of the serum calcium level in nephrectomized dogs was determined by noting the response to intravenously injected parathyroid hormone and by study of the oxalate tolerance. In 3 dogs the serum calcium level increased from 10 to 13 mg. per 100 ml., while no increase occurred in one dog which did not receive hormone. Dogs in which the thyroid and parathyroid glands had also been removed reacted in the same way if they were given sufficient amounts of the hormone. Sodium oxalate (40 mg. per kg.) caused a fall in serum calcium level with slow recovery to a normal value in both normal and nephrectomized dogs; this recovery did not occur in parathyroidectomized dogs. The view is expressed that the serum calcium level is not influenced by the kidneys.

H. Herxheimer

1787. The Probability that Compound F (17-Hydroxycorticosterone) is the Hormone Produced by the Normal Human Adrenal Cortex

J. W. CONN, L. H. LOUIS, and S. S. FAJANS. *Science [Science]* **113**, 713-714, June 22, 1951. 1 fig., 8 refs.

The metabolic effects of giving compound F, 400 mg. daily by mouth for 4 days, to a healthy volunteer have been studied. Excretion of sodium and of chloride was reduced and oedema developed. Excretion of nitrogen, sulphur, glucose, and uric acid were increased, and output of 17-ketosteroids and of 11-oxysteroids was doubled. Eosinophil cells were absent from the blood. The effects of ACTH administration were closely simulated. The only important difference between the actions of ACTH and of compound F was in the esterified serum cholesterol level, which was reduced by the former but was not affected by the latter. This difference is understandable if the esterified cholesterol of serum is a precursor of adrenal hormone.

Free compound F is as active intramuscularly as by mouth, but the acetate is relatively inactive when given intramuscularly, though active by mouth.

The authors consider that these findings are a strong indication that compound F is the substance normally secreted by the adrenal cortex when ACTH is administered.

C. L. Cope

1788. An Extra-adrenal Action of Adrenotropic Hormone
H. SELYE. *Nature [Nature, Lond.]* **168**, 149-150, July 28, 1951. 6 refs.

Previous experiments by the author have shown that stress causes involution of the thymus during the first stage of the "alarm" reaction. This can be prevented by adrenalectomy, but it occurs in the absence of the adrenal glands if adrenocortical extract is given. In the present experiment 120 female rats were divided into four groups and adrenalectomy was performed upon all of them. One group received hypertensinogen, which was used as representative of a non-hormonal protein;

of the other three groups, one received ACTH alone, one ACTH together with cortisone, and the other was given hypertensinogen with cortisone. In none of the groups did a significant loss of body weight occur. Neither ACTH nor hypertensinogen produced any significant involution of the thymus, and cortisone when given in conjunction with hypertensinogen caused only a mild degree of thymolysis; but cortisone and ACTH together caused a significant increase in thymus involution, as measured by weighing and confirmed by histological examination.

H. Herxheimer

1789. Neural Control of the Pituitary Gland. I. The Neurohypophysis. II. The Adenohypophysis, with Special Reference to the Secretion of ACTH

G. W. HARRIS. *British Medical Journal [Brit. med. J.]* **2**, 559-564 and 627-634, Sept. 8 and 15, 1951. 8 figs., bibliography.

NERVOUS SYSTEM

1790. The Presence of Histamine and Noradrenaline in Nerves as related to their Content of Myelinated and Unmyelinated Fibres. [In English]

B. REXED and U. S. VON EULER. *Acta Psychiatrica et Neurologica Scandinavica [Acta psychiat. scand.]* **26**, 61-65, 1951. 6 figs., 14 refs.

Fresh bovine nerves were extracted with acid alcohol or trichloroacetic acid and the extracts were tested biologically for their content of noradrenaline, adrenaline, and histamine. In addition, the relative amounts of thick and thin myelinated fibres and of unmyelinated fibres present in these nerves were determined histologically. The results indicated: (1) that the large myelinated fibres contain little or no histamine or noradrenaline; (2) that the higher the percentage of unmyelinated nerve fibres present, the larger is the amount of histamine and noradrenaline; and (3) that the unmyelinated autonomic nerves (post-ganglionic fibres of sympathetic origin) are the richest in histamine and noradrenaline.

G. B. West

1791. Repetitive Discharges in Human Motor Nerve Fibres during the Post-ischaemic State

E. KUGELBERG and W. COBB. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.]* **14**, 88-94, May, 1951. 6 figs., 15 refs.

After inflation of two cuffs placed on the upper arm and then release of the upper cuff, shock stimulation of the ulnar nerve was followed by a repetitive discharge in the first dorsal interosseous muscle. Similar results were obtained when rising currents were used to stimulate the ulnar nerve. The results were more consistent when one of the two cuffs was placed on the forearm. As spontaneous repetitive firing was still obtained after nerve block with lignocaine, the phenomenon cannot be due to reflex activity. It is concluded that the repetitive firing arises from the segment of nerve which has been released from ischaemia, and not from the neuro-muscular junction.

A. Schweitzer

1792. Dandy's Striatal Theory of "the Center of Consciousness". Surgical Evidence and Logical Analysis Indicating its Improbability

R. MEYERS. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 65, 659-671, June, 1951. 3 figs., 46 refs.

In 1930 Dandy asserted that the "centre of consciousness" was situated in the part of the brain that is irrigated by the anterior cerebral artery; in 1946, when the clinical evidence made this untenable, he postulated that it was to be found in the corpus striatum, more specifically in the oral portions of the head of the caudate nucleus and the putamen. He maintained that a lesion of these structures on one or both sides is followed by complete and permanent loss of consciousness.

The present author has operated upon 27 patients and removed portions of the striatum corresponding to, or exceeding, the limits of Dandy's centre. Three of these patients died without recovering consciousness; of the remainder, in 14 the extirpation was on the right side, in 9 on the left, and in 1 bilateral. None showed any characteristic enduring unconsciousness during the post-operative period. In the 3 patients who died, necropsy confirmed the site of the lesion. These cases, therefore, provided no factual support for Dandy's theory.

The author then subjects the original theory to a logical analysis [which, by taking it as a type specimen of much similar neurological speculation, provides the *raison d'être* of the paper and gives it especial value]. It is considered under four headings:

1. *Is the problem potentially solvable?* The assumptions implied by the hypothesis of Dandy are: (i) that the term "consciousness" symbolizes an unambiguous entity; (ii) that circumscribed anatomical brain "centres" exist within which such functions reside, and that "consciousness" is a function of this type and is therefore potentially locatable; (iii) that the use of the definite article "the" implies that one, and only one, cerebral centre exists to which consciousness is related. Common neurological experience shows at once that the concept of "consciousness" is difficult to define, as witness the numerous synonyms for it which are in use. The second tenet concerning the location of centres would also be denied by most modern neurologists, and it harks back through the nineteenth-century "diagram-makers" of Head's description to the theories of Franz Gall. [A similar lack of clear thinking on the supposed location of functions that have no physiological or logical existence has clouded a great part of the literature of aphasia.] In spite of the fact that the author establishes that the problem has no philosophical basis, he proceeds to discuss it further on more conventional scientific grounds.

2. *Are the "facts" on which the anterior-striatum theory is based reliable?* Critical inquiry into the cases presented as evidence reveals that the majority of "facts" are mere inferences, and that considerable doubt attaches to the remainder.

3. *Does the theory follow logically from the facts?* In regard to both aspects, whereby rival propositions are excluded and the striatum identified, there are shown to be many illogical inferences.

4. *Have subsequently disclosed facts sustained the predictions that arise from the theory?* On the basis of the cases reported the answer must be "No".

Donald McDonald

1793. Reflex Factors in Clonus and Tremor

M. H. CLARE, W. H. MILLS, and G. H. BISHOP. *Journal of Applied Physiology* [J. appl. Physiol.] 3, 714-731, June, 1951. 7 figs., 11 refs.

This investigation of the physiological factors determining the pattern of muscular contraction, with special reference to tremor, is based on experiments on 27 cats. After preliminary sedation with pentobarbitone sodium, ether was administered intratracheally and the saphenous and peroneal nerves were exposed and electrically stimulated at various stages of anaesthesia, with differing strengths of stimulus and at varying intervals.

It was found that a preliminary shock produced a brief period of facilitation of about 15 milliseconds, followed by a longer period of depression lasting from 0.1 to 0.3 second. The period of facilitation was encroached upon by the inhibitory phase with increasing depth of anaesthesia, so that a second shock, which had produced a second twitch under lighter anaesthesia, now failed to elicit a response, to produce which a stronger shock was required. If a series of shocks was administered at frequencies up to 1/16 second, strong shocks caused equal responses, but weaker shocks failed to elicit responses after the first, each successive shock inhibiting the next, even when it had produced no response itself. If the frequencies were shorter, responses occurred to every second, third, or fourth shock, while to weaker stimuli all but the first were completely inhibited.

Inhibition is thus augmented by increasing the first shock or by deepening anaesthesia, whereas increasing the subsequent shocks diminished or broke through the inhibition caused by the first. Decreasing the first shock, on the other hand, increased facilitation. Against a tonic background, single or repetitive shocks are each followed by the cycle of facilitation and inhibition. The inhibitory period can be induced by conditioning shocks activating not more than one-half of the first or beta component of the nerve potential, and sometimes by shocks too weak to elicit a muscular response.

In 3 cats subjected to decerebration under ether and allowed to recover from the anaesthetic the same types of curves of facilitation and inhibition were obtained as under anaesthesia alone without decerebration.

It is argued that this pattern of response explains the tremor of Parkinsonism, which, although induced by lesions at higher levels which increase muscular tone, derives its pattern from a typical cord clonic mechanism, which breaks the tonic activity into intermittent bursts. There is, therefore, no essential difference between Parkinsonian tremor and sustained clonus, both being imputed to a common factor of exaggerated reflex inhibition. The difference in reflex response of the spastic and of the rigid state may be that in the former the cord is specifically hyperexcitable though quiescent, while in the latter it is overtly excited.

L. Firman-Edwards

Pharmacology and Therapeutics

1794. **Absorption, Metabolism, and Excretion of "Parpanit" in the Body.** (Über Resorption, Abbau und Ausscheidung von Parpanit im Organismus)

R. PULVER. *Archives Internationales de Pharmacodynamie et de Therapie* [Arch. int. Pharmacodyn.] **86**, 185-202, April 1, 1951. 4 figs., 46 refs.

"Parpanit" concentration has been estimated photometrically after combination with methyl orange and extraction with ethylene dichloride by using the principle of the method of Brodie and Udenfriend (*J. biol. Chem.*, 1945, **158**, 705). Concentrations of from 0.1 to 5 mg. per 100 ml. can be determined with an error of $\pm 6\%$. Evidence has been obtained for the natural occurrence of an enzyme (parpanit-esterase) capable of splitting parpanit into diethylaminoethanol and phenylcyclopentonecarboxylic acid. Optimum pH and temperature for the activity of this enzyme are 8.75 and 50°C. respectively. It is inhibited by NaF or KCN and has been distinguished from other known serum and liver esterases. It is present in liver and kidney of rabbits, rats, and guinea-pigs, but is not always found in serum. Thus it was present in the serum of only 19 of 44 rabbits. No activity was found in the blood of any of 12 healthy human subjects.

A unit of parpanit-esterase activity is defined under standard test conditions. When parpanit, 0.2 g. per kg. of body weight, was injected subcutaneously in 5% solution into 4 rabbits with no detectable serum parpanit-esterase activity, toxic symptoms occurred associated with plasma concentrations of parpanit up to 3.6 mg. per 100 ml. After similar injections in 4 rabbits whose serum had parpanit-esterase activity *in vitro*, no symptoms occurred and blood levels of parpanit were not more than 0.1 mg. per 100 ml. Most of the injected parpanit is broken down in the body, less than 2% of it appearing unchanged in the urine in rabbits. In rabbits with high serum parpanit-esterase activity very little parpanit is present in the tissues 1 hour after subcutaneous injection. In other rabbits a high concentration may be present at that time—for example, in brain and heart muscle. In rabbits poisoned with carbon tetrachloride, chloroform, or white phosphorus, serum parpanit-esterase activity may increase, or appear if not previously present.

Derek R. Wood

1795. **Prolongation of Thiopental Anesthesia in the Mouse by Premedication with Tetraethylthiuram Disulfide ("Antabuse")**

N. J. GIARMAN, F. H. FLICK, and J. M. WHITE. *Science* [Science] **114**, 35-36, July 13, 1951. 4 refs.

In this investigation albino male mice of the Carworth Farms strain weighing 23 to 25 g. were selected at random and divided into three groups: Group 1 received no premedication; Group 2 received 25 mg. "antabuse" daily for 3 days before the experiment; while Group 3

were treated similarly to Group 2 except that the animals were given a preparation containing ferrous iron and ascorbic acid following administration of the anaesthetic. Anaesthesia was produced in the three groups by the intraperitoneal injection of 30 mg. per kg. of thiopentone, the end-point of the anaesthesia being the restoration of the righting reflex.

Antabuse was found to increase the duration of anaesthesia sixty-fold, but to produce this effect had to be given for 3 days before the experiment was carried out. The preparation of ferrous iron and ascorbic acid contained 27.5% $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ and 1.25% ascorbic acid in distilled water. Each animal of the third group was given 0.1 ml. of this solution intravenously. No reversal of the effect of the antabuse was obtained.

The authors infer that xanthine oxidase was one enzyme concerned in the metabolism of thiopentone to thiopentone carboxylic acid, and conclude that thiopentone should be given with caution to individuals undergoing treatment with antabuse. Norval Taylor

1796. **Experiments on the Role of Potassium in the Blocking of Neuromuscular Transmission by Curare and Other Drugs**

W. O. FENN, R. GERSCHMAN, G. FISCHER, J. LACY, M. D. BAILLY, and J. L. WRIGHT. *Journal of General Physiology* [J. gen. Physiol.] **34**, 607-617, May 20, 1951. 20 refs.

It has been postulated that acetylcholine formed at nerve-endings liberates K from an organic compound, RK, and that it is the liberated K which stimulates the muscle. It has also been postulated that curare acts by combining with the RK and liberating K. Thus no RK is available to the acetylcholine for the stimulation of the muscle.

In one series of experiments the muscles of the frog's hind limb were perfused with 3% acacia (dialysed) in Ringer's solution containing 10% of washed beef erythrocytes. A similar solution containing D-tubocurarine could be switched into the circuit. In this series of experiments there was no significant release of potassium by the D-tubocurarine. When Ringer's solution without the addition of erythrocytes or acacia was used the same result was obtained. Negative results were also obtained by the use of dihydro- β -erythroidine or "mephenesin" instead of D-tubocurarine. When acetylcholine in the presence of eserine was used instead of D-tubocurarine there was an average liberation of 0.45 mEq. of potassium per litre. When D-tubocurarine was added to the solution of acetylcholine the potassium liberated amounted to only 0.05 mEq. per litre.

In another series of experiments isolated frog muscles were soaked for periods varying from 3 to 8 hours in 200 ml. of Ringer's solution with and without the addition of curare, mephenesin, or acetylcholine. After soaking, the muscles were analysed for their potassium content.

Alternatively the muscles were immersed in 2 or 3 ml. of solution for varying periods of time and the potassium content of the solution was determined. With D-tubocurarine no consistent effect was obtained by either method, nor could any significant effect be detected with mephenesin or acetylcholine. It was concluded that there is no significant cation exchange between acetylcholine and potassium in muscle, but only a small loss of potassium due to the contracture produced by acetylcholine.

P. A. Nasmyth

1797. Relation of Rate of Excretion of Salicylate to Urinary Acidity. [In English]

P. L. DAVIS and P. K. SMITH. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **86**, 303-310, May 1, 1951. 1 fig., 15 refs.

It is known that if the urine is alkaline the rate of excretion of salicylate is increased. The experiments described show how the renal clearance of salicylate at different urinary pH values varies in comparison with that of thiosulphate in dogs. The clearance rate of thiosulphate is independent of urinary pH and is equal to the glomerular filtration rate. In urine of a pH less than 6.5 salicylate excretion is low. With increasing pH the rate of clearance of free salicylate increases and approaches that of thiosulphate. Salicylate is excreted by a filtration-reabsorption process, the amount of reabsorption decreasing in alkaline urine.

Derek R. Wood

1798. The Mode of Action of Morphine upon the Intestine

E. M. V. WILLIAMS and D. H. P. STREETEN. *British Journal of Pharmacology and Chemotherapy* [Brit. J. Pharmacol.] **6**, 263-272, June, 1951. 5 figs., 22 refs.

The authors studied the rate of transport of Tyrode solution in Thiry-Vella loops in conscious dogs under controlled conditions of temperature and pressure. Morphine was found to inhibit propulsion by closure of the intestinal lumen. If the pressure in the loop was increased or the gut relaxed by adrenaline or noradrenaline, transport would occur, only to stop when the pressure was allowed to fall or the effect of the adrenaline wore off. Atropine was found to antagonize moderate, but not large, doses of morphine. The relationship of these findings to previous work of the authors themselves and others is discussed.

Norval Taylor

1799. Effect on Experimental Gastric Ulcer in the Rat of Phenothiazine Derivatives, Particularly "Diparcol", "Parsidol", and "Phenergan". (Action sur l'ulcère gastrique expérimental du rat des dérivés de la phénothiazine et en particulier du diparcol, du parsidol et du phénergan)

M. MAROTTA and D. BOVET. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **86**, 117-184, April 1, 1951. 4 figs., 10 refs.

The authors, using the method of Shay, produced gastric erosions, ulcers, and perforations in rats following ligation of the pylorus under anaesthesia. The stomachs were examined 24 hours later. The substances tested for possible protective action were injected subcutaneously

in doses of 100 mg. per kg. of body weight before operation and again 6 hours later. In this dose "parsidol" [(N-β-diethylamino-β-methylethyl)-phenothiazine] prevented both ulceration and congestion in the stomach; when given in smaller doses it was less effective. "Diparcol" (diethazine) also prevented ulcer formation, but considerable hyperaemia persisted. The effect of the other compounds tested—"phenergan" (promethazine), "3015 R.P." [N-(β-diethylaminoethyl)-phenothiazine], and "3580 R.P." [N-(β-triethylaminoethyl)-phenothiazine ethiodide]—was much smaller in terms of the number of animals completely protected. However, all the drugs reduced by 71 to 92%, on an average, the number of ulcers in each animal. Tetraethylammonium iodide and hexamethonium iodide in the same dose had even less activity.

It was concluded that the relative ulcer-protective activities of the phenothiazine compounds parallel their relative activities in blocking the ganglionic-stimulant action of nicotine and do not appear to be correlated with either their antihistamine or their atropine-like potencies.

Derek R. Wood

1800. Effects of the Anti-histaminic Drugs on Tissue Reactions. [In English]

J. PEPYS. *Acta Allergologica* [Acta allerg., Kbh.] **4**, 115-149, 1951. 4 figs., 29 refs.

The author found that high doses of antihistaminic drugs in patients suffering from allergic rhinitis and polyposis were more likely than low doses to produce a decrease in cellular content and eosinophil infiltration. There seemed to be little correlation between the amount of clinical relief and degree of cellular infiltration. The prevention of the whealing reaction by antihistaminic drugs did not prevent the appearance of tissue changes normally found in allergic wheals, which suggests that the antigen-antibody reaction had taken place. Furthermore, the drugs prevented the enhancing effect of histamine and allergic wheals on the diffusion and absorption of substances from the skin. The author states that the ability of the antihistaminic drugs to inhibit the flare reaction seems to be related to the production of local analgesia.

A. W. Frankland

1801. Action of Histamine and of Leukotaxine on the Permeability and Granulopexy of the Vascular Endothelium. Essay on the Physiological Differentiation of Histamine and Leukotaxine with Particular Regard to the Effects Produced by Antihistaminic Drugs. [In English]

G. BIOZZI, G. MENÉ, and Z. OVARY. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **86**, 335-349, May 1, 1951. 5 figs., 25 refs.

According to this report from the University of Rome of experiments on guinea-pig skin, both histamine and leukotaxine have the property of increasing capillary permeability and also of stimulating the endothelial cells of small vessels to phagocytose injected indian ink (granulopexy). However, certain properties distinguish the two substances. Leukotaxine is active in higher dilutions than histamine. The granulopexy produced

by leukotaxine differs from that due to histamine in that there is a great accumulation of leucocytes inside and outside the vessels and some perivascular phagocytosis. These actions of histamine, but not those of leukotaxine, are antagonized by low concentrations of mepyramine ("neointergan") and promethazine ("phenergan"). It requires much larger concentrations to inhibit the effect of leukotaxine—probably due to a direct action of the antihistaminics on the endothelial cells. Leukotaxine has no histamine-like activity on isolated guinea-pig intestine. It is concluded that "leukotaxine acts without the intervention of any histamine mechanism".

Derek R. Wood

1802. The Effects of Magnesium on Cardiac Arrhythmias caused by Digitalis

P. SZEKELY and N. A. WYNNE. *Clinical Science [Clin. Sci.]* 10, 241-253, 1951. 6 figs., 20 refs.

This paper presents clinical and experimental observations in support of the claim that magnesium sulphate is of therapeutic value in abolishing extrasystolic bigeminy and ventricular tachycardia caused by digitalis. Of 11 patients with cardiac arrhythmia precipitated by digitalis, 6 were given an intravenous injection of 15 to 20 ml. of a 20% solution of magnesium sulphate, with the following results: bidirectional ventricular tachycardia was interrupted in 2 cases and extrasystolic bigeminy abolished in 4 cases; in all but one case this effect was permanent.

The experimental investigation was carried out on a number of cats in which cardiac arrhythmia was induced by large doses of digitalis or strophanthin. Administration of magnesium sulphate in small doses either restored sinus rhythm or, more commonly, caused a slow idio-ventricular rhythm. In 4 instances of extrasystolic bigeminy this was abolished by giving magnesium in doses of 0.25 to 0.5 ml.

The depressant action of magnesium on myocardial conduction and irritability persists after atropinization and vagotomy; it can therefore be said that magnesium has a direct action on the cardiac muscle.

A. I. Suchett-Kaye

1803. The Effect of Priscoline on Peripheral Blood Flow in Normal Subjects and Patients with Peripheral Vascular Disorders

T. B. VAN ITALLIE and C. W. CLARKE. *Circulation [Circulation]* 3, 820-829, June, 1951. 2 figs., 10 refs.

The authors studied 28 subjects by digital plethysmography before and after reflex heating and before and after intravenous injection of tolazoline ("priscoline"). The subjects were in 4 groups: normal, patients with vasospastic disorders, patients with occlusive arteritis, and patients who had undergone sympathectomy. The resting digital blood flow was found to be much less in the vasospastic group than in the normal or in the organic group, in which the flow was less than in the normal subjects. The post-sympathectomy patients had a high resting flow. After tolazoline the flow was increased fivefold in the normal subjects, tenfold in the vasospastic cases, but only twofold in the organic group; similar

changes occurred in the digital pulse volume. After sympathectomy a slight but definite increase in digital flow and pulse volume followed the administration of tolazoline.

After body heating alone the increases in digital flow and pulse volume were less than after tolazoline alone in all groups. After reflex heating and tolazoline administration together the normal group showed a fourfold, the vasospastic cases a thirteenfold, and the organic cases a twofold increase in digital blood flow. No serious toxic effects followed tolazoline injection, except for postural fainting in an 83-year-old subject.

The authors conclude that although the patients with organic disease had a lower resting flow than normal subjects, the presence of organic arteriolar changes may best be revealed by the failure of the flow to increase after reflex heating and/or tolazoline injection. Tolazoline administration and reflex heating produced comparable increases in flow and exhibited some additive effect when used together. The maximum increase in flow produced by reflex heating is considered to be a reproducible standard against which the effect of vasodilator substances can be measured.

J. F. Goodwin

1804. The Effect of Epinephrine on the Pulmonary Circulation in Man

A. C. WITHAM and J. W. FLEMING. *Journal of Clinical Investigation [J. clin. Invest.]* 30, 707-717, July, 1951. 5 figs., 27 refs.

In this study 13 fasting patients were given 0.1 or 0.2 g. of sodium phenobarbitone intramuscularly to produce sedation. Pulmonary arterial catheterization was performed with an intracardiac catheter, and all systemic arterial blood samples and pressure records were obtained from an indwelling femoral arterial needle. A preliminary injection of Evans blue dye was made and several pressure tracings were taken. Then 0.5 to 0.7 ml. of 1 in 1,000 adrenaline was injected intramuscularly, and the blood pressure was closely followed. From 2½ to 10 minutes later a second dye injection was made, and in each case the blood pressure was followed until its return to normal. In addition, 0.025 mg. of adrenaline was given intravenously on 6 occasions.

The most consistent effect of adrenaline on the lesser circulation was a rise in pulmonary arterial pressure; the diastolic pressure was not increased. The moderate increase in cardiac output was insufficient to account for the rise in pulmonary arterial pressure, but in some cases it appeared that an increase in pulmonary vascular resistance was the primary cause.

G. B. West

1805. The Effect of Nor-epinephrine upon Pulmonary Arteriolar Resistance in Man

N. O. FOWLER, R. N. WESTCOTT, R. C. SCOTT, and J. MCGUIRE. *Journal of Clinical Investigation [J. clin. Invest.]* 30, 517-524, May, 1951. 2 figs., 17 refs.

In an attempt to determine how noradrenaline produces pulmonary arterial hypertension in man, measurements of pulmonary arterial and capillary pressure, of cardiac output, and of brachial arterial pressure were

obtained in 12 patients before, during, and 10 minutes after a continuous infusion of 0.2 to 0.4 μ g. L-noradrenaline per kg. per minute. Increased pulmonary arterial and brachial arterial pressure, increased resistance, diminished cardiac output, and bradycardia resulted. In all cases noradrenaline produced an increase in pulmonary capillary pressure equal to the mean increase in pulmonary arterial pressure. Hence it is concluded that the usual mechanism whereby noradrenaline produces pulmonary hypertension in man is through an increase in pulmonary capillary or venous pressure and not through constriction of pulmonary arteries.

G. B. West

1806. The Comparative Action of Certain Ganglionic Blocking Agents. [In English]

J. L. MORRISON, C. HEYMANS, A. P. RICHARDSON, and H. A. WALKER. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **86**, 203-213, April 1, 1951. 5 figs., 13 refs.

Tetraethylammonium bromide (TEA), "parpanit", "diparcol" (diethazine), and bis-(γ - γ -2-trimethylammoniumpropyl ether) dihydrochloride ("MC 2444") are commonly known as "ganglionic blocking agents". In this investigation their relative activities in various tests were studied.

In comparing the effects of these substances on the reflex bradycardia which occurs after adrenaline injection, it appeared that TEA was the least active of the four blocking agents. However, this assessment ignores the fact that both parpanit and diparcol are potent adrenergic agents in the doses used. The test is suitable only for comparing the activities of TEA and MC 2444. Similarly, only these two substances can satisfactorily be compared for their effect in causing a postural hypotension when the animal is tilted. In the anaesthetized, atropinized dog with both vagi cut parpanit and diparcol blocked the "nicotinic" pressor action of acetylcholine more readily than they blocked the pressor response to occlusion of the carotid artery. With TEA the carotid reflex was more easily blocked. Here again the adrenergic action of parpanit and diparcol complicated their action on the ganglia.

The authors point out that the relative activities of these substances in blocking the effects of vagal stimulation on heart rate and blood pressure do not represent ganglionic blocking action only. Relative activities estimated in this test were: TEA, 1.0; diparcol, 3.6; parpanit, 9.0; and MC 2444, 1.2. The high activity of parpanit is largely due to its atropine-like action and not to blockade of the vagal synapses.

In the discussion the authors emphasize the need for a complete study of the relative sensitivity of different ganglia to such substances and of their other actions.

[It is useful to stress the fact that the descriptive classification, for convenience, of a substance as "ganglionic blocking agent", or "atropine-like", or "antihistaminic", should not lead those who use it to regard its action as necessarily confined to that suggested by the description, even in therapeutic doses.]

Derek R. Wood

1807. Action of Trihexylphenidyl (Artane) and Atropine on Central Synaptic Transmission. [In English]

C. HEYMANS, J. E. HYDE, and P. TERP. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **86**, 215-219, April, 1 1951. 3 figs., 6 refs.

In an investigation to determine whether "artane" has any effect on transmission through medullary centres the authors, using the perfused isolated head preparation, induced hypertension in the donor dog (A) and in the perfused head of dog B, causing a reflex bradycardia in the trunk of dog B by way of the vagus nerves, the only connexion between the head and trunk of dog B. In each of three experiments neither 10 mg. of atropine per kg. of body weight nor 2 mg. of artane (benzhexol), which has considerable atropine-like activity, had any effect on this reflex bradycardia. Atropine also failed to prevent in dog B the bradycardia due to direct stimulation of the cardio-inhibitory centre by the anaemia resulting from occlusion of the carotid arteries. This is further evidence against the operation of the same mechanism for both central and peripheral autonomic transmission.

Derek R. Wood

1808. The Interrelationship of Vitamin K and Dicoumarin

G. E. COLLENTINE and A. J. QUICK. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **222**, 7-12, July, 1951. 1 fig., 24 refs.

To study the relationship between dicoumarol and vitamin K, experiments were carried out on dogs which had been subjected to cholecystectomy. A standard dose of dicoumarol of 1 mg. per kg. body weight was given and the standard dose of vitamin K₁ chosen was 10 μ g. per kg. body weight. Three synthetic compounds were tested: 2-methyl-1:4-naphthoquinone ("menadiolone"), 2-methyl-1:4-naphthohydroquinone trisodium sulphate ("hykinone"), and 2-methyl-1:4-naphthohydroquinone diphosphoric ester tetrasodium salt ("synkavite"). These were compared with vitamin K₁ on the basis of their molecular weights.

It was found that a dog's susceptibility to dicoumarol steadily increased as the body store of vitamin K became depleted. When dicoumarol and vitamin K were given simultaneously in the ratio of 100 to 1 to a dog depleted of its vitamin store the two agents mutually opposed each other. The marked hypoprothrombinaemia produced by a small dose of dicoumarol was promptly corrected by administration of vitamin K and the synthetic compounds.

It is postulated that dicoumarol acts as an anti-vitamin. Vitamin K combines with an apoenzyme to form an active enzyme (AEK) which is responsible for the synthesis of prothrombin. Dicoumarol will also combine with the apoenzyme to form an inactive AED which prevents the formation of AEK. The following equilibrium occurs: $AEK + D = AED + K$. The factors which influence this equation are the relative affinities of dicoumarol and vitamin K for the apoenzyme, the store of vitamin K and of dicoumarol in the organism, and the ability of the body to excrete or inactivate dicoumarol.

A. W. H. Foxell

CHEMOTHERAPY

1809. The Mode of Action of Antrycide

W. E. ORMEROD. *British Journal of Pharmacology and Chemotherapy* [Brit. J. Pharmacol.] 6, 325-333, June, 1951. 4 figs., 4 refs.

In all the experiments described a strain of *Trypanosoma equiperdum* was used in rats and mice. *In vitro* "antrycide" had little trypanocidal action, although after 20 hours' incubation at 37° C. in a concentration of the drug of 1 in 640,000, trypanosomes lost their infectivity. There was no detectable difference in normal and resistant strains either in their response to the trypanocidal action of antrycide or in their loss of infectivity. Some degree of inhibition of respiration was observed at a concentration of 1 in 40,000 by the use of the Warburg technique; again no difference was observed with the resistant strain. The author concludes that there is no connexion between the therapeutic effect of the drug and the trypanocidal effect and inhibition of respiration observed *in vitro*, since the necessary drug concentrations were much higher than those achieved *in vivo*.

In the blood of infected mice dosed with antrycide there is the natural increase in parasitaemia for 24 to 48 hours and then a decrease brought about by the drug; the infectivity of trypanosomes in a mouse treated with an effective dose (0.1 mg. per 20 g.) becomes markedly reduced as early as 45 minutes after dosing.

Morphological changes noted after dosing were a decrease in the proportion of dividing forms late in the experiment, and the appearance of deeply staining inclusion bodies in the cytoplasm of the trypanosome. These bodies appeared in 24 hours and could be seen in the living trypanosome by phase-contrast microscopy and as bright spots in a fluorescence photomicrograph; they did not appear to impede the trypanosome in any way and did not appear in trypanosomes of a resistant strain. *T. rhodesiense* from a mouse given 0.01 mg. per 20 g. readily produced multinucleate forms with up to as many as six nuclei.

It is postulated that antrycide acts as a growth inhibitor, acting primarily on the cytoplasm rather than the nucleus, after slowly penetrating the cell membrane.

I. M. Rollo

1810. A Study of Basophilic Inclusion Bodies Produced by Chemotherapeutic Agents in Trypanosomes

W. E. ORMEROD. *British Journal of Pharmacology and Chemotherapy* [Brit. J. Pharmacol.] 6, 334-341, June, 1951. 22 refs.

This paper presents a more detailed study of the deeply staining inclusion bodies found in trypanosomes after "antrycide" treatment (Abstract 1809). These may occur: (a) after treatment of the host with antrycide, dimidium bromide, or suramin; (b) on the addition of basic vital stains such as neutral red to the trypanosome-suspending fluid; or (c) as naturally occurring "volutin" granules. Those produced by method (a) are permanent, while those resulting from (b) are reversible, the basophilic granules disappearing shortly after the suspending fluid is washed clean.

Blood films from mice infected with *Trypanosoma equiperdum* and treated with antrycide were further investigated cytochemically. Stained with Unna's carbol-pyronin-methyl-green the inclusion bodies were orange-red, indicating—though this is not wholly specific—that they possibly contain ribose nucleic acid. After incubation at 30° C. in twice-distilled water containing (a) crystalline ribose nuclease or (b) protease-free crystalline ribose nuclease or (c) crystalline trypsin and staining with Giemsa, the following effects were observed: method (a) removed the inclusion bodies completely; method (b) altered their appearance so that they became more eosinophilic and less basophilic than controls; method (c) had no effect. These results, coupled with confirmatory tests [for which the original should be consulted], show that the chief constituents of the inclusion bodies are probably ribose nucleic acid and protein.

The author postulates that antrycide, like dimidium bromide and suramin, having a molecule which is permanently charged, is retained in the trypanosome, while the charged forms of vital stains are in equilibrium at pH 7.5 with uncharged forms which can diffuse rapidly through the trypanosome membrane. Some of the simpler nucleoproteins are broken down by double decomposition either with acids or bases, at least *in vitro* and probably in the trypanosome cytoplasm, into their constituent proteins and ribose nucleic acids. This occurs with antrycide, dimidium bromide, and suramin, and with vital stains, the reaction with the first three being permanent and with the last reversible, resulting in inhibition of the growth and division of the trypanosomes.

I. M. Rollo

1811. Studies in the Chemotherapy of Cholera—V. Effects of Oral Administration of Pteridines, Sulphonamides and their Mixtures to Mice

H. O. J. COLLIER and I. F. HALL. *Annals of Tropical Medicine and Parasitology* [Ann. trop. Med. Parasit.] 45, 51-57, May, 1951. 10 refs.

This paper is the fifth in a series dealing with the chemotherapy of cholera by certain 2:4-diaminopteridines. The compound 2:4-diamino-1'-methylindolo-(2':3'-6:7)-pteridine was found to be the most useful, since, though it was comparatively non-toxic when administered orally to mice it conferred high vibriostatic activity on the faeces. When the compound was mixed with "formo-cibazol" or sulphaguanidine a synergistic effect was obtained.

R. Wien

1812. Studies in the Chemotherapy of Cholera—VI. Protection by Pteridines of Mice Infected with *Vibrio cholerae*

H. O. J. COLLIER and I. F. HALL. *Annals of Tropical Medicine and Parasitology* [Ann. trop. Med. Parasit.] 45, 58-61, May, 1951. 5 refs.

In continuation of the investigation reported in the previous paper in the series (Abstract 1811) it was found that 2:4-diamino-1'-methylindolo-(2':3'-6:7)-pteridine, when administered intraperitoneally as the phosphate, gave some protection to mice infected with *Vibrio*

cholerae, but did not protect when given by mouth. Another compound, 2:4-diamino-6:7-diisopropylpteridine, was effective when administered orally and also had some effect when given intraperitoneally. Both compounds were less effective than chloramphenicol. The authors point out that the degree of activity of these compounds against an infection in mice may not be the same as that in man, since *V. cholerae* multiplies in quite different sites in the two species.

R. Wien

ANTIBIOTICS

1813. *In vitro* and *in vivo* Studies of a New Antibiotic, Fumagillin, with *Entamoeba histolytica*

A. K. HRENOFF and M. NAKAMURA. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N. Y.] 77, 162-164, May, 1951. 8 refs.

A new antibiotic—fumagillin, or "antibiotic H-3"—was tested for its effect on *Entamoeba histolytica* both *in vitro* and *in vivo*. The amoebicidal end-point of this antibiotic *in vitro* was determined on cultures of *E. histolytica* associated with *Trypanosoma cruzi*, as previously described by the authors. Fumagillin, being insoluble in water alone, was dissolved in N/100 NaOH. Cultures investigated were 48 hours old and incubated at 37° C. The effect on these cultures of the alkalized solution of fumagillin in serial dilutions was examined by further incubation at 37° C. for 48 hours in the presence of this antibiotic. Subcultures were made from all the tubes in which amoebae were not demonstrated.

For control purposes the antibiotic in amoebicidal concentrations was tested against trypanosomes alone and was found to be ineffective; the solvent (N/100 NaOH) alone was not toxic for amoebae. The amoebicidal concentration of fumagillin was in the region of 1 in 10,000,000 to 1 in 15,000,000.

The trial of fumagillin *in vivo* was carried out on *Macacus mulatta* and *M. philippinensis* naturally infected with *E. histolytica*: 14 monkeys were given daily by mouth for 5 days 50 to 125 mg. of the antibiotic per kg. of body weight. In 4 of the animals *E. histolytica* reappeared in the stools in 4 to 12 weeks, but of the other 10 no *E. histolytica* were subsequently found in 4 after 14 weeks, in 5 after 8 weeks, and in one after 4 weeks (the last animal died of tuberculosis).

Results of the bromsulphalein test suggest that a dose of 125 mg. per kg. might cause liver damage. In one monkey given 100 mg. per kg. the blood urea nitrogen level was increased. Electrocardiograms from all animals were normal.

For examination of the faeces smears were made within 30 minutes after passage of the stool, fixed in Schaudinn's fluid, and stained by Heidenhain's iron-haematoxylin method. During the follow-up period of examination after treatment 2 smears from each monkey were searched for protozoan parasites on 5 consecutive days every 2 weeks.

The effect of fumagillin on non-pathogenic amoebae could not be evaluated, as these were present in the stools of only 3 of the monkeys tested. However, the fact that

in 2 of the animals *Entamoeba coli* disappeared during the 14-week follow-up period led the authors to conclude that the drug may also be effective *in vivo* against non-pathogenic amoebae.

J. W. Czekalowski

1814. The Occurrence of Antibacterial Substances in Seed Plants with Special Reference to *Mycobacterium tuberculosis*

E. H. LUCAS, A. LICKFELDT, R. Y. GOTTSALL, and J. C. JENNINGS. *Bulletin of the Torrey Botanical Club* [Bull. Torrey bot. Cl.] 78, 310-321, July-Aug., 1951. 1 ref.

A series of 199 plants were tested for antibacterial activity *in vitro* against *Mycobacterium tuberculosis*, *Staphylococcus aureus*, *Salmonella typhi-murium*, and *Bacterium coli*. Twenty-three plants showed an inhibitory action on the growth of *Myco. tuberculosis*: the most active were leaves of *Buxus sempervirens*, *Chrysanthemum segetum*, *Lupinus polyphyllus*, *Syringa vulgaris*, *Rosa canina*, and *Taxus canadensis*. Activity was present in the flowers of *Salix caprea*, *Rosa canina*, *Primula malacoides*, *Syringa vulgaris*, *Barbarea vulgaris*, and in the roots of *Petasites japonicus*, *Chamaecyparissus*, *Lupinus hirsutus*, and *L. polyphyllus*. The leaves of *Tulipa gesneriana* showed some activity against *Staph. aureus*, *Salm. typhi-murium*, and *Bact. coli*.

G. M. Findlay

1815. Effectiveness of a New Compound, Benemid, in Elevating Serum Penicillin Concentrations

J. M. BURNELL and W. M. M. KIRBY. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 697-700, July, 1951. 12 refs.

The rapid renal clearance of penicillin makes it difficult to maintain blood levels adequate to combat resistant organisms. Substances which block renal tubular excretion of penicillin have been shown to raise the blood level, but only caronamide has been extensively used. The new compound *p*-(di-*n*-propylsulphamyl)-benzoic acid ("benemid") also enhances the blood level of penicillin by a similar action.

In this investigation to test the effectiveness of benemid in raising the serum penicillin level 74 adult patients in the King County Hospital, Seattle, were divided into five groups according to the dosage of penicillin received. Group 1, consisting of 19 patients receiving 300,000 units of procaine-penicillin intramuscularly once daily, were given benemid in doses of 0.5 g. every 6 hours for at least 24 hours before the serum level of penicillin was measured. The level before and after giving benemid was measured in each patient at 3, 12, and 24 hours following a penicillin injection. Of the 57 occasions on which comparisons were made, a threefold increase in the penicillin level following benemid was noted 39 times. In Group 2, of 27 patients receiving the same dose of penicillin every 12 hours, the serum level was measured before, 3 hours after, and 12 hours after a penicillin injection. There was, on an average, a 2.5-fold increase in the penicillin level following benemid on 50 occasions of the 54 when determinations were compared. A similar increase was noted in Group 3,

containing 5 patients receiving 600,000 units of procaine-penicillin every 8 hours. Group 4 consisted of 19 patients who were receiving 100,000 units of crystalline benzyl penicillin every 3 hours. The blood penicillin level following benemid was higher in 18 of the cases, the average increase being threefold. Group 5 consisted of 4 patients receiving 1,000,000 units of crystalline penicillin every 2 hours, in whom the serum penicillin level was measured 2 hours after an injection of penicillin. On an average, the serum level was increased by benemid from 21 units per ml. to 73 units per ml. The cerebrospinal-fluid level of penicillin in 2 of these patients was raised about 20 times.

Nearly all the patients received 2 g. benemid daily for 2 or 3 days, and in none was there any evidence of systemic toxicity. It thus appears that the oral administration of 0.5 g. of benemid every 6 hours may give a three- to five-fold enhancement of the serum penicillin level without producing any toxic signs or symptoms.

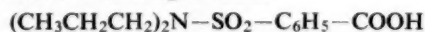
[If later work on more patients confirms the above findings, it seems certain that benemid will prove of value in oral penicillin therapy.]

G. B. West

1816. Oral Administration of Procaine Penicillin with and without Benemid *p*-(Di-*n*-propylsulphamyl) Benzoic Acid

W. F. WALKER and R. B. HUNTER. *Lancet* [*Lancet*] 2, 104-106, July 21, 1951. 3 figs., 11 refs.

As is well known, the administration of caronamide during penicillin treatment blocks the excretion of penicillin by the renal tubules and increases the concentration in the blood. However, the use of caronamide is attended by various disadvantages, and this has restricted its adoption to the exceptional case, such as in resistant bacterial endocarditis. The present paper describes another compound having a similar action—"benemid", which has the following formula:



This is a crystalline white powder, nearly insoluble in water, and tasteless. It is rapidly absorbed from the gastro-intestinal tract, but very slowly excreted by the kidneys. Dogs have been given 200 mg. per kg. of body weight daily for 6 weeks without ill effects. In man a dose of 2 to 4 g. per day is effective and safe. It seems to inhibit various enzyme systems which are involved in the excretion of a number of drugs by the renal tubules and it raises the blood levels of penicillin and of *p*-aminosalicylic acid.

The present paper describes an investigation in which it was attempted to obtain a satisfactory concentration of penicillin in the blood by administering penicillin by mouth with, in addition, 0.5 g. of benemid 6-hourly. Three preparations of penicillin were tried, 7 to 10 patients receiving each of them. One of the preparations—a penicillin ester, L.G.2—yielded only very low blood levels and obviously was unsuitable for oral administration. Procaine-penicillin (0.5 g.), on the other hand, yielded fairly high levels (about 0.6 unit per ml., at 1 to 2 hours), and so did sodium benzyl penicillin. The patients were then given benemid 0.5 g. 6-hourly for 24

hours, after which the administration of procaine-penicillin was repeated. The resultant blood concentration of penicillin was 2 to 4 times as great as that without benemid, and its duration was correspondingly increased. On the other hand, there was a great variation between different patients in the blood level attained after the oral administration of penicillin, so that the significance of the findings is difficult to check statistically. Benemid caused no untoward symptoms. Some patients took it continuously for 42 days without ill effect, and tubular function (as judged by phenolsulphonephthalein excretion) returned to normal within 24 hours of stopping the drug.

F. Hawking

1817. Vascular Changes in Tuberculous Meningitis after Treatment with Streptomycin. (Sulle alterazioni vascolari della meningite tubercolare trattata con streptomycin)

V. BARBERA. *Rivista di Anatomia Patologica e di Oncologia* [*Riv. Anat. patol.*] 4, 449-512, April, 1951. 52 figs., bibliography.

In this paper from the Institute of Morbid Anatomy and Histology of the University of Bari the author reports the results of his study of the vascular changes found in the central nervous system in 15 cases of tuberculous meningitis treated with streptomycin. He was able to confirm the reports of other authors as to the great frequency with which vascular changes occur in this disease. These changes appeared to be the same as those occurring in non-treated cases, especially those which followed a protracted course. The picture was, however, more diffuse, with the superimposition of exudative, granulomatous, necrotic, and reparative changes in various combinations. The arterial changes were characterized by a greater polymorphism, especially of the intima. During the initial phase the smaller vessels were affected, while at a later stage the process extended to the larger vessels. Among the latter those of the Sylvian fossa were involved to a greater extent than those of the base of the brain. Diffuse and serious involvement of the larger arteries indicates that the disease has run a protracted course. The veins showed less polymorphism than the arteries. The most frequent change was lymphoid degeneration of the vessel walls. Their reaction to granulomatous and necrotic changes in the surrounding tissues was found to be fundamentally passive. There was no sign of intimal reaction and very little fibrosis.

The vascular changes of tuberculous meningitis seriously hinder recovery with complete cure, which is possible only at a very early stage of the disease. The author concludes that these changes, especially when the arteries are involved, owing to their gravity and progressive character, represent the gravest obstacle to complete recovery. He assumes that, although the treatment with streptomycin was successful in controlling exudation, the reparative process, particularly in the region of vessels, can have very grave consequences. The fact that the process spreads from the small vessels to those of larger calibre indicates that the best results can be obtained in the initial phases. The author also

raises the question of the irritating influence of streptomycin when administered intrathecally. The presence of irritation in cases treated by injections into the cistern could be demonstrated experimentally in animals. The degree of irritation appeared to be in proportion to the amount of streptomycin injected. Although it is known that streptomycin does cause irritation, there is no evidence that the irritation is greater than that caused by other substances administered intrathecally. The author did not find any appreciable difference between the cases treated intrathecally and those in which general measures were applied.

E. Forrai

TOXICOLOGY

1818. **Toxic Reactions on the Labyrinthine Reflexes, caused by Tetra-ethyl-thiuramdisulphide.** [In English] J. BRUG and A. B. H. FUNCKE. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **87**, 113-117, July, 1951. 3 refs.

Tetraethylthiuramdisulphide is used in the treatment of alcoholism. A pure crystalline sample prepared by the authors had an LD 50 of 2.5 g. per kg. of body weight when given by stomach-tube to guinea-pigs. Commercial samples were more toxic, perhaps because of finer subdivision and more rapid absorption.

Acute toxic symptoms in guinea-pigs were: fall of temperature, loss of weight, "strained" respiration, and ataxia. One animal which survived a dose of 2 g. per kg. recovered, but 4 weeks later the static labyrinthine head reflexes, compensatory eye positions, and nystagmus on rotation had disappeared. The animal was also ataxic and deaf; no improvement took place during 5 months.

Single doses of 1.5 or 1 g. per kg., a course of 14 daily doses of 0.5 or 0.1 g. per kg., and a course of 5 doses of 1 g. per kg. at 2-day intervals all had similar effects, except that the kinetic reflexes did not disappear and no deafness was observed. Some animals recovered in 6 to 8 weeks. No gross anatomical changes were observed in the affected animals, but histological examination of the labyrinth and eighth nerve have not yet been made. The authors have so far received from only one clinician a report of cases of ataxia following overdose of the drug in man.

L. G. Goodwin

1819. **Antidiuretic Effect of Nicotine and its Implications** J. H. BURN. *British Medical Journal* [Brit. med. J.] **2**, 199-201, July 28, 1951. 11 refs.

The author reviews the evidence which has accumulated from work done in the Oxford laboratories and elsewhere in the last few years on the effects of smoking or of injections of nicotine on the posterior pituitary body. It is quite clear that smoking a cigarette causes the release of enough antidiuretic hormone from the pituitary gland, probably as a result of stimulation of the supra-optic nuclei, to inhibit diuresis for a variable but not inconsiderable time. Since the antidiuretic hormone and the vasopressor hormone are probably one, the question arises whether or not enough of this substance is released by smoking to affect the coronary flow in man. From a

careful comparison and correlation of results obtained by measuring the effect of smoking, of injecting nicotine, and of injecting posterior-lobe extract on water diuresis in man it has been shown that smoking releases certain measurable quantities of posterior-lobe extract or its equivalent. From direct measurements of coronary flow in dogs it has also been shown that such amounts of nicotine reduce the coronary flow. The conclusion is that smoking probably reduces coronary flow and is therefore contraindicated in cardiac disease.

James D. P. Graham

1820. **Therapeutic Possibilities in "Parathion" Poisoning.** (Thérapeutische Möglichkeiten bei der Parathion-Vergiftung)

G. WILHELM and R. DOMENJOZ. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **86**, 321-334, May 1, 1951. 30 refs.

The toxic potentialities of the insecticide "parathion" are reviewed. Those using it may complain of headache and lassitude. In severe poisoning, symptoms of excessive parasympathetic stimulation are seen, including sweat rash, lacrimation, salivation, nausea, vomiting, diarrhoea, intestinal colic, dyspnoea due to bronchospasm, myosis, and paralysis of accommodation, with a fall in body temperature. Muscular tremors and convulsions may precede coma and cardiovascular collapse. At necropsy oedema of lungs and brain is seen, together with generalized capillary dilatation.

The experiments reported in this paper were carried out on mice to test the effectiveness of various substances which might be expected to be therapeutically useful. These included eserine, "artane" (benzhexol), "trasentin", phenobarbitone, morphine, phenytoin, tubocurarine, "diparcol" (diethazine), "phenergan" (promethazine), and sympathol. Of these only artane gave significant protection. Atropine and "parpanit" were more effective than any of the above drugs; they were more effective against poisoning by intravenous than by oral parathion. Parpanit was most effective against intravenous parathion. Parpanit, 10 to 20 mg. per kg. injected intraperitoneally, reduced mortality due to intravenous parathion from 5 in 10 to 0 in 10. When the parathion was administered orally the antidotes were only effective if given repeatedly.

The results emphasize the need for early treatment and indicate that the prevention of further absorption of parathion from skin, mucous membranes, or stomach is most important. Injection of atropine sulphate is recommended. Parpanit, with its wider activity (against the nicotine-like actions of acetylcholine as well), should also be given, especially if atropine is not well tolerated. At present it can be given only orally or rectally in the form of crushed tablets.

[As potential antidotes, other "ganglionic blocking agents" which also possess atropine-like activity, such as "banthine", should be investigated.]

Derek R. Wood

1821. **Toxic Hepatitis from para-Aminosalicylic Acid** G. D. W. MCKENDRICK. *Lancet* [Lancet] **2**, 668-669, Oct. 13, 1951. 7 refs.

1822. Acute Aniline Poisoning in Infancy. (L'avvelenamento acuto da anilina nell'infanzia)

L. PARENZAN and G. ZARBIN. *Minerva Pediatrica* [Minerva pediatri., Torino] 3, 393-398, July, 1951. 47 refs.

The authors give details of 3 cases of aniline poisoning in young children aged 3, 2½, and 1½ years respectively. All were caused by drinking unknown quantities of a commercial pigment solution containing aniline. The symptoms were intense cyanosis, tachycardia, vomiting, and collapse; in one patient, who was afebrile, convulsions occurred. The main therapeutic measure employed was injection of 500 mg. of ascorbic acid and infusion of 100 ml. of whole blood or glucose saline. Recovery took place in a few days without complications.

Other features of the syndrome of aniline poisoning are the marked and characteristic methaemoglobinemia (the transformation of haemoglobin to methaemoglobin is brought about by an intermediate product of aniline metabolism—*para*-aminophenol); tachypnoea with signs of anoxaemia; low blood pressure; albuminuria, casts, and bile pigments in the urine; and ketonuria. Frequently characteristic pigment granules (Heinz bodies) can be demonstrated in blood films.

These findings, combined with a history of possible consumption of a noxious agent, usually render elucidation of the differential diagnosis of states of cyanosis not too difficult, providing the paediatrician keeps in mind the possibility of this type of poisoning.

James D. P. Graham

1823. Laburnum Poisoning in Children. Report of Ten Cases

R. G. MITCHELL. *Lancet* [Lancet] 2, 57-58, July 14, 1951. 1 fig., 11 refs.

Although the laburnum is extensively grown in Great Britain and elsewhere, few references to laburnum poisoning have appeared in the medical literature during the past 25 years. The poisonous alkaloid cytisine is present in all parts of the tree, the content in the bark and flowers being fairly constant, whereas that in the pods varies considerably as seasonal concentration into the seeds takes place. Cytisine stimulates and then paralyses autonomic ganglia, and has a central emetic action; it is excreted by the kidney. Fatal cases have occurred, but the lethal dose has not been determined.

From recent records of the Royal Hospital for Sick Children, Edinburgh, the author has extracted 10 cases, in children of 3 to 10 years, which were all due to eating laburnum pods or seeds during the months of July, August, or September. The main clinical features, which usually began within half an hour of ingestion, were: repeated vomiting (in all), marked pallor (7), rapid pulse (7), drowsiness (6), weakness and incoordination (4), and mydriasis (4). No diarrhoea was recorded and no rise in temperature above 98.8° F. (37.1° C.). All the patients recovered. Details are given of 2 cases, in the first of which a boy of 7 had eaten two laburnum pods and, half an hour later, had started vomiting copiously; he was pale, pulse 120 to 144 per minute, and pupils dilated. In the other case a boy of 4½ had

eaten laburnum seeds and almost immediately had become "tottering and weak, with dilated pupils and rolling eyes". He was shocked and nearly pulseless when seen by his doctor, who gave an emetic and an injection of nikethamide. After vomiting he improved, but on admission to hospital his pulse rate was 120, he was drowsy, and his pupils were dilated. In each case gastric lavage had a good effect, and both patients were discharged the following day.

Laburnum poisoning may prove fatal, and requires immediate treatment. The first measure is gastric lavage and may suffice; nikethamide or other stimulants should be given where there is much depression; artificial respiration may be required. An adequate intake of fluids should be ensured in order to assist elimination of cytisine by the kidneys.

V. Reade

INDUSTRIAL TOXICOLOGY

1824. Arsinic: Electrocardiographic Changes produced in Acute Human Poisoning

C. J. JOSEPHSON, S. S. PINTO, and S. J. PETRONELLA. *Archives of Industrial Hygiene and Occupational Medicine* [Arch. industr. Hyg. occup. Med.] 4, 43-52, July, 1951. 4 figs., 16 refs.

Electrocardiograms were obtained in 10 of 13 cases of arsine poisoning, the clinical details of which were described previously (*Arch. industr. Hyg. occup. Med.*, 1950, 1, 437). The first records were made 36 to 48 hours after exposure to arsine, and recordings were repeated at intervals for periods up to 18 months. In all cases except one, high-peaked T waves occurred, particularly in the precordial leads near the sternum (CF₂), becoming less at CF₄ and least marked at CF₆. The T-wave elevation was present in the limb leads, though not to such a high degree. Maximum elevation occurred between 48 and 96 hours after exposure in 7 cases, while in the remainder it appeared after 5, 7, and 12 days respectively. In 8 out of 10 cases the maximum elevation of the T wave in CF₂ and CF₄ occurred on the same day. In 7 cases the S-T segment had an elevated take-off in the precordial leads, which was maximal at 36 to 48 hours, and returned to normal in 96 hours, after exposure. In one man the records did not conform with the pattern common to the others, in that the T wave showed late inversion in all records. This change persisted for 18 months, though the degree of inversion decreased. It is postulated that this was due to changes in the myocardium immediately beneath, or extending into, the pericardium.

Hyperpotassaemia is discussed as a possible cause of the electrocardiographic changes. Potassium is released from the erythrocytes as a result of haemolysis, and although serum potassium determinations were not made, it is suggested that the occurrence of haemoglobinuria would be an indication of possible hyperpotassaemia. The results show that the typical electrocardiographic changes appear whether or not there is clinical haemoglobinuria. In addition to this argument, it is pointed out that no widening of the QRS complex or narrowing of

the base of the T wave was seen, as would be expected in potassium intoxication.

In the 4 cases that ended fatally death was due clinically to acute myocardial failure, while necropsy in 2 of these cases revealed extensive myocardial degenerative changes. These changes are considered to be due either to the direct action of arsine on the tissues or to the action of arsine metabolites derived from haemolysing erythrocytes. In conclusion, it is suggested that these electrocardiographic changes are the most sensitive means of diagnosing arsine poisoning yet discovered.

W. K. S. Moore

1825. **The Toxicity of Selenium Anhydride.** (О токсичности селенистого ангидрида)

B. C. FILATOVA. Гигиена и Санитария [Gigiena] No. 5, 18-23, May, 1951. 3 figs.

The formation in the atmosphere of selenium anhydride (SeO_2) may originate in the technical preparation of selenium used in the manufacture of such commodities as electrical appliances. Interest in this gas was aroused when it was discovered that it had a marked effect upon the respiratory tract and nervous system. Investigation confirmed this finding. The author carried out experiments on white rats and studied their behaviour when states of acute and chronic intoxication had been induced.

When subjected to concentrations of 0.15 to 0.6 mg. per litre (5 to 17.5 mg. per kg. body weight) the rats first showed conjunctival irritation and respiratory distress; they became restless and started rubbing their noses with their paws. After 15 to 20 minutes they began to gasp, threw back their heads, and, as restlessness increased, attempted to scale the walls of the chamber. The pupils dilated, convulsions set in, and the rats died in from 1 to 4 hours. Post-mortem examination revealed severe damage to the respiratory organs, indicated by oedema of the lungs. Liver, spleen, kidney, and heart showed signs of degeneration. Evidence of the effect of SeO_2 on the nervous system was given by the convulsions.

The effects of chronic intoxication were estimated from the aspect of the rats during the test, the change in weight, and the alterations in the blood picture. When subjected to a concentration of 0.01 to 0.03 mg. of SeO_2 per litre the rats lost weight, anaemia and conjunctival irritation developed, and drowsiness set in. Death occurred within 8 to 18 days. Necropsy revealed similar changes in the respiratory tract and parenchymatous organs to those present in acute intoxication. The effects of exposure to lower concentrations of the gas were much less pronounced.

Compared with other industrial poisons SeO_2 is more toxic than hydrogen phosphide and has approximately the same toxicity as phosgene. To confirm her experimental findings the author carried out an investigation on industrial premises. She found that when the concentration of the gas in the air was 0.00078 mg. per litre or greater, signs that the nervous system was affected were shown by the workers. She therefore recommends that the concentration of SeO_2 in the atmosphere should not exceed 0.0003 mg. per litre.

E. S. Fountain

1826. **Studies on the Mechanism of Acute Beryllium Poisoning**

K. W. COCHRAN, M. M. ZERWIC, and K. P. DuBOIS. *Journal of Pharmacology and Experimental Therapeutics* [J. Pharmacol.] 102, 165-178, July, 1951. 29 refs.

The intraperitoneal injection of beryllium chloride in rats and guinea-pigs, with subsequent observation for 30 days, showed that, calculated as beryllium, it has an LD 50 of 0.56 mg. per kg. of body weight for rats and 6.3 mg. per kg. for guinea-pigs. In view of this marked difference between these two species in susceptibility to beryllium, tissues from both were used to ascertain whether a correlation between species susceptibility and phosphatase inhibition existed. The normal alkaline-phosphatase activity of the various homogenized tissues was measured and the concentration of beryllium required to produce 50% inhibition of hydrolysis of β -glycerophosphate determined. The tissues examined were: serum, liver, duodenum, kidney, thyroid gland, adrenal cortex, and adrenal medulla. With the exception of the adrenal cortex and medulla, the tissues of the rat had a higher alkaline-phosphatase activity than those of the guinea-pig and, with some exceptions, the enzyme was more sensitive to beryllium poisoning.

To correlate these results with experiments *in vivo*, intraperitoneal injections of beryllium were given at various dose levels and the alkaline-phosphatase activity of different tissues was estimated at various times after the injections. The activity of the enzyme in rat serum was markedly inhibited, and the inhibition persisted throughout the survival time after lethal doses, but was reversible after sublethal doses. The phosphatase activity of kidney and duodenum was also inhibited *in vivo*, while the activity of other tissues was not appreciably inhibited. Manganese, cobalt, nickel, zinc, yttrium, and lanthanum afforded some protection against the inhibition of phosphatase *in vitro*, but failed to afford any protection in experiments *in vivo*. The adenosine-tri-phosphatase activity of tissues was inhibited by beryllium *in vivo*, but the activity of glucose-6-phosphatase and 5-nucleotidase was unaffected. Phosphoglucomutase activity of liver and skeletal muscle was inhibited *in vivo* and *in vitro*, and this effect was antagonized by magnesium. The liver and kidney of beryllium-poisoned rats showed a decrease in content of phosphocreatine and adenosine triphosphate and a marked increase in inorganic phosphorus content. Glucose-1-phosphate content was increased and glucose-6-phosphate content decreased.

P. A. Nasmyth

1827. **The Effect of 2:3-Dimercapto-propanol (BAL) on Experimental Nickel Carbonyl Poisoning**

J. M. BARNES and F. A. DENZ. *British Journal of Industrial Medicine* [Brit. J. industr. Med.] 8, 117-126, July, 1951. 10 figs., 25 refs.

1828. **Failure of Oral D.D.T. to Induce Toxic Changes in Rats**

G. R. CAMERON and K. K. CHENG. *British Medical Journal* [Brit. med. J.] 2, 819-821, Oct. 6, 1951. 6 refs.

Medical Jurisprudence

1829. **The Toxicological Use of Irradiation for the Detection of Arsenic and the Study of its Distribution in the Hair.** (Utilisation en toxicologie de la radioactivité provoquée de l'arsenic pour la détection et l'étude de la répartition de cet élément dans les cheveux)

H. GRIFFON and J. BARBAUD. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences [C. R. Acad. Sci., Paris]* **232**, 1455-1457, April 9, 1951. 1 fig., 3 refs.

In chronic arsenic poisoning the metal is deposited in the hair, and chemical analysis of successive lengths of the hair is important in determining the time when poisoning began. Analytical procedures necessitate the destruction of the hair; and quantitative estimation can be made only on portions of hair several millimetres long and involving at least 3 to 4 weeks of growth. The authors have tried to devise a method without those disadvantages. The procedure consists in making the metal in the hair artificially radioactive by exposing it to a flow of neutrons and then measuring the radiations from the hair. The element can be determined by its period, and its position identified along the length of the hair. The acquired radioactivity is plotted on a graph against the length of the hair. Minerals normally present are of course rendered radioactive, but this radioactivity in normal hairs produces a straight-line graph. The presence of abnormal quantities of arsenic is shown by undulations in the curve. The reliability of the method was checked chemically.

Gilbert Forbes

1830. **Phosphatase in Dried Seminal Stains**

J. S. FAULDS. *Edinburgh Medical Journal [Edinb. med. J.]* **58**, 94-98, Feb., 1951. 3 figs., 3 refs.

For a chemical test of seminal fluid to be conclusive it would have to be based on the presence of some substance in the fluid which is not present in other body fluids, or is present in them in minute amounts only, compared with the quantity in semen. Prostatic secretion contains much acid phosphatase compared with other tissue fluids, but the author found that once the fluid had become a dried stain on cloth the enzyme disappeared quickly, though total disappearance took about 14 months, depending on the original concentration of the phosphatase and the conditions under which the stained cloth was stored.

The author also found that the concentration of acid phosphatase in the semen of animals is infinitesimal compared with that in human semen. The average for man is 2,500 King-Armstrong units per ml., while the author's highest reading for animals was 12 units. [This observation might be of value in determining whether a seminal stain could possibly be of animal origin, but the precipitin test would be more definite and reliable.] In the author's view, when any stain contains 5 units of phosphatase per square centimetre of cloth a seminal

stain should be suspected: if it contains 10 units or more it is certainly a seminal stain. A control from the unstained cloth was employed. The author also applied this method to vaginal swabs.

Gilbert Forbes

1831. **Unexpected Death in Infants and Young Children: Second Series**

K. M. BOWDEN and E. L. FRENCH. *Medical Journal of Australia [Med. J. Aust.]* **1**, 925-933, June 30, 1951. 7 figs., 13 refs.

This paper describes the post-mortem findings in 43 children who died suddenly, many of them being found dead in bed. In 29 cases history revealed evidence of minor ill-health for several days or weeks. At necropsy, bacteriological cultures were obtained from swabs of the nasal contents and of material from the base of the brain and from specimens of pericardial fluid, heart blood, liver, spleen, and lung. The authors believe that there is no rapid invasion of the tissues by bacteria from the alimentary canal within the first few days of death, and that post-mortem bacteriological studies represent a true picture of the condition during life.

By a combination of morbid anatomical, and bacteriological investigation an adequate cause of death of an infective nature was found in 14 cases. There was a group of 20 cases in which histological evidence of respiratory-tract infection was found, but the organism was not identified. In only 2 cases was a meningococcal infection proved, though in 7 others it was suspected, in spite of negative cultures.

In the authors' view the seasonal incidence of these unexpected deaths suggests that respiratory infection may be an important factor. Their findings tend to support the contention that many cases of sudden death in infants which are labelled "accidental suffocation in bed" can in fact be proved to be cases of natural death if an energetic investigation is carried out.

Gilbert Forbes

1832. **Age and Putrefaction.** (Età e putrefazione)

D. CAVALLAZZI. *Minerva Medico-legale [Minerva medicoleg.]* **71**, 59-62, May-June, 1951. 8 figs., 14 refs.

Pieces of liver were removed at necropsy, performed within 48 hours of death on patients without any morbid condition. The specimens were kept in running water at 17° C. for 11 days and pieces were taken for section every second day. The liver tissue could still be recognized in many sections from the liver of younger subjects after 13 days, but in elderly subjects identification became difficult after 6 to 8 days. Nuclear and cytoplasmic changes in the cells were seen to be more severe at a much earlier stage in the older age groups.

E. Neumark

Radiology

EXPERIMENTAL

1833. The Localisation of Cerebral Tumours with Radioactive Derivatives of Fluorescein. Physical Limitations

E. H. BELCHER and H. D. EVANS. *British Journal of Radiology* [Brit. J. Radiol.] **24**, 272-279, May, 1951. 6 figs., 2 refs.

This paper, from the Physics Department of the Royal Cancer Hospital, London, is concerned with the physical limitations of the method of locating cerebral tumours by means of intravenously injected radioactive diiodofluorescein and a Geiger-Müller counter placed externally to the intact skull. If 2% of the injected activity (maximum permissible, 1 mc. ^{131}I) is present a few hours after injection in the brain (weight approximately 1,400 g.) and there is an increase in concentration in tumour by a factor of 10, the physical problem concerns the detection of inclusions of ^{131}I with an activity of 0.14 $\mu\text{c.}$ per ml. in a medium with an activity of 0.014 $\mu\text{c.}$ per ml.

On account of its greater efficiency a scintillation counter was employed, and was surrounded by a lead collimator to give directional properties. The apparatus and its calibration are discussed. A phantom skull was used for the experimental observations; the brain tissue was simulated by a gelatin medium containing ^{131}I , and the tumours by cylindrical glass vessels containing ^{131}I and embedded in the gelatin medium. In each case counting rates were measured from a number of standard positions.

It is calculated that the concentration in the normal brain (0.014 $\mu\text{c.}$ per ml.) following an injection of 1 mc. diiodofluorescein will give a counting rate of 30.5 counts per second. With a background of 32.5 counts per second this gives a total counting rate of 63 counts per second. If it is possible to detect a 20% increase in this value, the smallest detectable region of increased concentration of activity will increase the rate by 12.6 counts per second. Such a counting rate is given by a point source of 5 $\mu\text{c.}$ at the centre of the brain; assuming a concentration in tumour tissue 10 times that in normal brain, the smallest detectable tumour in the centre of the brain would measure $5 \div 0.14 \text{ ml.} = 36 \text{ ml.}$ If the centre of the tumour were 5 cm. below the surface this volume would be reduced to 14 ml. In practice, however, distribution in normal brain, owing to the variability of the vascular pattern, is not likely to be uniform, so that detection of a 20% change in counting rate is likely to be difficult, and an assumed concentration factor of 10 in brain tumour may be an optimistic figure. Nevertheless it would appear possible with the present apparatus to locate large-concentration lesions by this method, particularly when these are close to the skull.

Certain improvements in counter design to increase efficiency, and the relative merits of diiodofluorescein and

dibromofluorescein, are described. The synthesis of these substances is described.

Edward M. McGirr

1834. Some Preliminary Clinical Observations on the Use of Radioactive Isotopes for the Localization of Brain Tumours

J. G. DE WINTER. *British Journal of Radiology* [Brit. J. Radiol.] **24**, 280-284, May, 1951. 6 figs., 15 refs.

The work described in this paper was carried out by the author and his collaborators at the Royal Cancer Hospital, London. Radioactive diiodofluorescein was injected intravenously, and advantage was taken of the selective ability of brain-tumour tissue to combine with it to determine the location of brain tumours by means of a scintillation Geiger-Müller counter applied externally to the intact skull (see Abstract 1833).

In the clinical investigations 1 mc. of ^{131}I as diiodofluorescein was used in all cases except 2, in which dibromofluorescein was given. A grid system was designed to allow symmetrical readings on both sides and at the front and back of the head. Counting was begun immediately after the injection in the initial cases, but as it became clear that differences in counts between tumour and control areas did not become apparent until 2 to 4 hours had elapsed, counting was not begun in the later cases until 2 hours after the injection. In all, 34 suspected cases of cerebral tumour were investigated. In positive cases it was found that the counting rates were markedly raised over the whole of the skull, but in only 1 of 20 confirmed cases could the site and extent of the tumour be traced with accuracy. A positive result was obtained in 1 of 14 unconfirmed cases, probably a case of angioma.

The author concludes that the method fails to provide any information of value regarding the position and size of cerebral tumours in the majority of the cases investigated. He considers that the vascularity of the brain has a greater influence on counting rates than the activity absorbed in tissue, and suggests that the method may prove useful for physiological investigations.

Edward M. McGirr

1835. Further Studies on Recovery from Radiation Injury

L. O. JACOBSON, E. L. SIMMONS, E. K. MARKS, E. O. GASTON, M. J. ROBSON, and J. H. ELDREDGE. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] **37**, 683-697, May, 1951. 12 refs.

In this paper the authors describe a number of experiments designed to determine the factors responsible for the rapid recovery of the haematopoietic system, the reduced mortality, and the enhanced recovery of the gastro-intestinal tract following 1,025 r whole-body x-radiation in the spleen-shielded mouse. Only 1.1%

of the mice survived 1,025 r whole-body exposure without spleen-shielding, whereas up to 77.7% survived this dose with spleen-shielding. Haematopoietic recovery from radiation injury was equally hastened by spleen-shielding in guinea-pigs, rats, and rabbits, but the survival rate was not increased to the same degree as in mice. Liver, head, or intensive shielding also reduced mortality, but not to the extent observed when the spleen was shielded. Surgical extirpation of the shielded spleen at intervals after the procedure indicated that the therapeutic effect derived from the shielded spleen had already been exerted in a few hours, and its removal thereafter did not interfere materially with the recovery process. Survival was likewise significantly enhanced by transplantation of 1 to 4 fresh spleens from young mice into the peritoneal cavity of irradiated mice immediately after exposure. This is taken to indicate that the responsible factors are definitely effective after irradiation and that their presence is unnecessary during the actual irradiation.

The assumption made in all these experiments on mice was that either a cellular or a non-cellular substance originating in the shielded tissues is responsible for the beneficial effect on the recovery of the irradiated animal. The evidence presented points in the direction of a non-cellular humoral substance, but the possibility that irradiation produces a "toxin" which inhibits regeneration and which in turn is neutralized by shielded tissue has not been entirely disproved by the experiments reported.

Jan G. de Winter

1836. Functional and Structural Changes Consequent to High Dosages of Radioactive Iodine

A. GORBMAN. *Journal of Clinical Endocrinology* [J. clin. Endocrinol.] 10, 1177-1191, Oct., 1950. 12 figs., 16 refs.

The dose of radioiodine required to destroy the thyroid gland in mice depends on the diet: mice fed on a diet with added potassium iodide retained only 1% of the dose in the gland, and 500 μ c. had little or no effect; with a more normal diet 8% of the dose was retained and 200 μ c. destroyed the gland; while with a low-iodine diet the uptake was 58% and 28 μ c. was the thyroid-lethal dose. Allowing for these different rates of uptake, it is calculated that the thyroid-lethal dose is 15 μ c. within the gland, or 4 μ c. per mg. of thyroid tissue.

The peak value of iodine accumulation may give a misleading impression of the effective dose of radioactivity because the higher doses are accumulated more rapidly and also dissipated more rapidly; this is attributed to damage to the iodine-retaining mechanisms of the gland. Thus the biological half-life (which would be the same as the physical half-life of 8 days if all the iodine taken up by the gland were retained there) is in fact about 2½ days with doses that fail to destroy the gland, about 1½ days with doses that do destroy it, and up to about 2 days with higher doses. These facts can be interpreted thus: thyroid-lethal doses destroy the capacity of the gland to retain iodine, but higher doses also interfere with the blood flow, so that retention becomes obligatory.

The course of the destruction with thyroid-lethal doses is this: nuclear pyknosis and some intrafollicular bleeding occur several days after dosing and there is swelling of the endothelium of the blood channels; gradually the pyknotic and necrotic tissue is removed by invading leucocytes and macrophages and the whole is replaced by fibrous tissue. Some cells and follicles survive for longer periods, but eventually disappear within 4 to 6 weeks; before this they appear moribund, with shrunken nuclei and cytoplasm, or show "colloid degeneration"—that is, nuclear pyknosis with gross swelling of the cytoplasm, which contains colloid-like droplets. With larger doses the destruction is more rapid. With smaller doses (3 μ c. per mg.) recognizable thyroid tissue often remains in the apices and isthmus of the gland, which are so small in the mouse that much of the ionization must occur beyond their limits. Three months after dosing a few clumps of atypical follicles or atypical cells in a state of "colloid degeneration" remain, but there is no neoplasia, metaplasia, or regeneration; the functional capacity of the gland is decreased, so that iodine storage is about 1% of normal and the little iodine that is retained is stored in the colloid.

With such a small gland as that of the mouse, the range of ionization (2 mm.) includes adjacent structures such as the trachea, thymus, and parathyroid glands. In a small proportion of cases the tracheal epithelium is denuded, and its regeneration (usually as abnormal squamous epithelium) is accompanied by proliferation of the tunica propria to form nodular fibromata that may partly or wholly occlude the trachea. Parathyroid damage was not usually fatal except with doses above the thyroid-lethal level or in especially susceptible strains of mice.

A more common and eventually fatal outcome of the thyroid destruction was the formation of chromophobe-cell pituitary tumours like those produced by excess oestrogen. These tumours were, however, unrelated to the sex of the mouse, being still producible in gonadectomized mice. The treatment tended to upset the oestrous cycle irregularly: predominance of oestrous or di-oestrous phases was equally produced. The female mice were rendered sterile by destruction of the ovarian oocytes, as after x-irradiation of the ovaries. The testes were unaffected.

The intrathyroid doses producing these effects were 4 to 20 times greater than those required in the treatment of human hyperthyroidism.

Peter C. Williams

RADIOTHERAPY

1837. Nasopharyngeal Irradiation. Relative Merits of Roentgen and Radium Therapy for Benign Conditions

L. H. GARLAND, H. A. HILL, M. E. MOTTRAM, and M. A. SISON. *Journal of the American Medical Association* [J. Amer. med. Ass.] 146, 454-460, June 2, 1951. 4 figs., 21 refs.

In this paper, in which the merits of radium and x-ray treatment of benign conditions are compared, the authors begin by considering the anatomy of the naso-

pharynx and Eustachian tubes, especially in relation to the distribution of lymphoid tissue. This, they state, is absent in and around the normal tube, but may occur in the presence of inflammation.

In discussing the pathology of Eustachian and pharyngeal inflammation they postulate hypertrophy of the lymphoid tissue around and even along the tube. Lymphoid tissue in the nasopharynx atrophies after puberty, but tends to persist in inflammatory conditions and acts as a focus of infection. Symptoms ranging from catarrh and postnasal discharge to Eustachian block and barotrauma occur. The condition is not amenable to surgery, and irradiation offers a good alternative. This can be applied by means of radium in the nasopharynx or external x-ray therapy.

Various technical methods of applying radium to the nasopharynx with special applicators are described and attention is drawn to the disadvantages, which include rapid fall-off and uneven distribution of dose, together with excessive dosage to tissues near the radium. This is especially true of those techniques where the β -radiation is not adequately screened off. External x-ray therapy is advocated as the treatment of choice. No anaesthesia is required; the dose is more homogeneous and the whole of the inflamed tissues can be easily included in the beams. No "hot-spots" need occur. The authors give 6 treatments of 100 to 150 r at weekly intervals with conventional apparatus to each of two fields of about 50 sq. cm. centred over the temporomandibular joint. No skin changes were found over a period of 20 years.

The results of others, as reported in the literature, are reviewed, and the authors advise "gentle" x-ray therapy as the treatment of choice. Of 720 patients treated by them 60 to 90% had relief of symptoms after one course of treatment.

[It is not generally agreed that lymphoid tissue may occur in the Eustachian tube in these conditions. Some authorities hold that the beneficial action of irradiation in such cases is due to its effect on the chronic inflammatory process, as seen in similar conditions elsewhere.]

R. D. S. Rhys-Lewis

1838. Carcinoma of the Hypopharynx. A Clinical Study of 322 Cases, Treated at Radiumhemmet from 1939 to 1947. [In English]

F. JACOBSSON. *Acta Radiologica [Acta radiol., Stockh.]* 35, 1-21, Jan., 1951. 4 figs., 28 refs.

In this study carcinomata of the hypopharynx arising below the level of the upper border of the cricoid have been classified separately from those arising above this level; the latter group includes extrinsic laryngeal and pyriform-fossa growths. In about three-quarters of the cases the tumour was in the lower hypopharynx, and 80% of these were in females. In 90% of the women and 10% of the men definite signs and symptoms of sideropenia appeared. For diagnosis of carcinoma in cases where the growth is in the lower hypopharynx endoscopic and radiological examination may be required; in one-sixth of cases in this series the tumour was invisible on indirect laryngoscopy. In 45% of cases the tumour

was more than 5 cm. in length; clinical lymph-node metastases were present in 54% of cases, and in about one-half of these the growth was inoperable. Well-differentiated squamous-cell carcinoma was the predominant histological type, poorly differentiated growths being found in one-third of cases in which the tumour was situated in the upper hypopharynx, but in only one-tenth of those where the growth was in the lower part.

Fractionated x-ray therapy is considered the treatment of choice. The patient should be treated in a sitting position, and beam direction by fluoroscopy used to avoid unintentional irradiation of the cervical cord. A four-field technique should be employed, with fields of 3.5 to 4 cm. width extending from the lower jaw down to, or even several centimetres below, the clavicle. The following are the factors used: 180 kV, 0.5 mm. Cu, 60 cm. F.S.D., surface intensity 50 r per minute; one field should be treated each day with a skin dose of 400 to 500 r. Tumour doses should be calculated from a transverse section of the neck at the centre of the tumour. A tumour dose of 5,700 to 6,000 r should be given over about a month; this will result in a second-degree epidermitis with some areas of exudative dermatitis, and a fibrinous mucosal reaction. A dose of 6,600 r or more over 4 weeks is considered to be beyond tissue tolerance. Supplementary telerradium is sometimes used in the presence of lymph-node metastases.

The importance is stressed of care of the patient's general condition, and of the use of penicillin and local naphthylmethylimidazole hydrochloride and N-cetylpyridine chloride in the treatment of acute pharyngolaryngeal oedema. A late irradiation change which may simulate recurrence of growth occurred in some of the cases treated. Dysphagia was complained of 5 months or more after irradiation, and radiologically there was increased thickness of the prevertebral shadow and an irregular mucosal contour. However, direct pharyngoscopy and biopsy revealed only oedema and fibrinous epithelitis, and the changes disappeared spontaneously in 1 to 2 months.

Results of treatment have been calculated for all treated cases, although in one-third of them it was impossible to give full treatment. The 5-year cure rate for the years 1939-42 was 7%; after fluoroscopic beam direction was instituted in 1943 the 5-year cure rate became 14% for cases treated between that date and 1945. An analysis of cases treated in 1948 and 1949 suggests that a 5-year-cure rate of about 20% is possible with the present technique. The results for carcinoma of the upper hypopharynx were 10% of 5-year cures, and for lower (post-cricoid) carcinoma 17%—a significant improvement in a group of cases generally regarded as of unfavourable prognosis.

Arthur Jones

1839. Roentgen Rotation Therapy in Cancer of the Hypopharynx. [In English]

I. GYNNING. *Acta Radiologica [Acta radiol., Stockh.]* 35, 443-448, May-June, 1951. 4 figs., 3 refs.

The neck is regarded as less suitable for x-ray rotation therapy than the thorax: however, the method can be applied to tumours not extending below the 7th cervical

vertebra in the absence of metastases. Until recently few patients had been so treated.

The author reports 5 patients treated before 1943; 2 of these are well 7 years after treatment—both were women with the Plummer-Vinson syndrome. The tumour doses are estimated at 5,200 r in 26 days (4×7 cm. field) and 5,200 r in 24 days (5×10 cm. field). Recovery from post-irradiation effects was also good in these 2 cases. The article is illustrated by striking radiographs taken before and after treatment.

J. L. Dobbie

1840. Roentgen Rotation Therapy in Cancer of the Esophagus. Dosage Problems. Preliminary Results. [In English]

I. GYNNING. *Acta Radiologica* [*Acta radiol., Stockh.*] 35, 428-442, May-June, 1951. 11 figs., 20 refs.

This paper deals with the measurement of tumour dose, the choice of dose, and the results of treatment both as a whole and in relation to dosage. The rate of tumour dosage under fixed treatment conditions is determined directly in each case by means of bougies containing ionization chambers. If there is good agreement, 4 to 5 measurements are enough in the course of each treatment.

After some clinical trials it appeared that the optimum dose lay between 6,500 r in 35 days and 6,800 r in 40 days. This is a high level of dosage and some complications of overdosage must be expected. The treatments reviewed number 88, all being in cases without clinical evidence of metastases, given in the 4 years 1943-7. Of the total patients treated, 52 died within a year of treatment and 10 lived for 2 years or more; among the latter were one 6-year and four 5-year survivals. Metastases accounted for 7 deaths without signs of local recurrence, and in 4 other fatal cases necropsy showed no sign of the primary tumour.

J. L. Dobbie

1841. Investigation of the Effect of X-radiation on the Localization of Radioactive Phosphorus in Breast Tumours F. ELLIS, C. HOCH-LIGETI, and R. OLIVER. *British Journal of Cancer* [*Brit. J. Cancer*] 5, 45-53, March, 1951. 6 figs., 3 refs.

Experiments were undertaken to investigate possible changes in the phosphorus content of malignant tumours during and after x-ray therapy and to correlate such changes with irradiation reactions in the tumour. As the penetration of beta rays into the tissues is only about 3 mm., only cases in which the mammary tumour was attached to the skin were selected. Tracer doses of 150 μ c. of ^{32}P were given, and the uptake was measured on marked sites over the tumour and corresponding points over the opposite normal breast. X-ray therapy up to a tumour dose of 3,400 r was applied in 4 cases and superficial x-ray therapy up to 2,500 r was given in one case.

The uptake of ^{32}P as measured by a Geiger-Müller counter was 3 to 8 times higher over malignant tumours attached to the skin than over the healthy breast. A high count was also obtained in the remote parts of the diseased breast. The exponential rate of disappearance of ^{32}P was similar on both the diseased and the normal

sides, but on the diseased side a sudden fall in count rate occurred in cases receiving x-ray treatment. This fall was noted first over the peripheral part of the breast and later over the tumour.

These findings suggest that they are due to the same mechanism as that described by Hevesy and Holmes in rats; that is, to changes in the metabolism of tumour cells or to vascular damage. High counts were obtained during the skin-reaction phase, so that after-treatment measurements should be postponed until the erythema has subsided.

I. G. Williams

1842. A New Method for the Treatment of Cancer of the Lungs by Means of Artificial Radioactivity (Zn^{63} and Au^{198}). First Experimental and Clinical Studies. [In English]

J. H. MULLER and P. H. ROSSIER. *Acta Radiologica* [*Acta radiol., Stockh.*] 35, 449-468, May-June, 1951. 10 figs., 12 refs.

The authors claim that they first demonstrated the selective fixation of a radioactive isotope in the lungs in 1946. They used radioactive zinc injected intravenously in a non-soluble form. In combination with radiotherapy at 400 kV this caused regression of the primary growth in one case with generalized metastases. It was decided that if radioactive gold could be prepared in such a way that particles of ^{198}Au of the same dimension as ^{63}Zn could be made available they would be selectively absorbed, and a special gold precipitate was evolved by an ingenious method of adsorption by charcoal powder.

Among the cases treated was one of generalized Hodgkin's disease affecting the lungs in which the serous exudate required repeated aspiration. Exudation ceased after injections of ^{198}Au , and autoradiography showed selective fixation of the isotope in the lungs. The patient is still alive. In 3 other cases, all of bronchial carcinoma, no significant improvement followed radioactive-gold therapy.

The very skilful methods by which the suspensions of gold were injected are described and show the possibilities of using a technique of transvenous catheterization of the heart to direct the gold particles to the tumour-bearing tissue. Unfortunately, the conditions which are suggested as likely to benefit are those in which palliation can usually be obtained by external irradiation carefully applied.

M. C. Tod

1843. Individualized Interstitial Irradiation of Cancer of the Uterine Cervix Using Cobalt 60 in Needles, Inserted through a Lucite Template. A Progress Report

J. L. MORTON, A. C. BARNES, G. W. CALLENDINE, and W. G. MYERS. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] 65, 737-748, May, 1951. 7 figs., 25 refs.

The authors, believing that interstitial irradiation offers advantages in the treatment of certain tumours, decided to use radioactive cobalt (^{60}Co) in the form of "cobanič" (an alloy of 45% cobalt and 55% nickel) for this purpose. Preliminary animal experiments had shown the biological effects of ^{60}Co to be similar to those of radium irradiation, but animal experiments are of

limited value in determining the clinical effects of the interstitial use of ^{60}Co , and it was decided that human application must be tried. Advanced cancer of the uterine cervix was chosen because, in theory, multiple needle implantation "gives the optimum possibility for uniform irradiation of cancer tissues", and a guided-needle technique was adopted. Cases in Stages 3 and 4 only were treated, and careful preliminary urological and radiological surveys were made.

The technique developed by the authors is as follows. "Lucite" templates are designed to fit in the vagina, being positioned by a central guide which enters the cervical canal. The needles are inserted through holes in the template so arranged that they form a geometrical pattern, and consist of stainless steel sheaths loaded with cylinders of radioactive cobalt with spacing pieces of aluminium or graphite. Treatment begins with external irradiation, the dose being 2,000 r in air to each of 2 anterior and posterior fields from ports of 15×20 cm. to 20×20 cm. in 20 days. This is followed by the insertion of cobalt needles.

Nine cases have been treated—all recently. Oedema of the vagina and labia developed about 2 weeks after treatment and persisted for about 4 weeks. Proctitis and cystitis have not been troublesome. One patient developed a typical rectal reaction. Puncture of the bladder occurred in one case and was suspected in another.

The doses from a standard applicator at chosen points are given and show that in the region of the lateral pelvic needle the dose is 10,956 r in $5\frac{1}{2}$ days. Just beyond this, on the lateral pelvic wall, it is 6,600 r. [This, being presumably additional to the dose received from external irradiation, is high dosage.]

M. C. Tod

1844. A Five Year Summary of X-ray Therapy of Arthritis, Bursitis, and Radiculitis

L. J. GELBER. *International Record of Medicine [Int. Rec. Med.]* 164, 62-78, Feb., 1951. 29 refs.

The author reports his experience in the x-ray treatment of over 900 cases of arthritis, bursitis, and radiculitis in the course of the last 5 years. His results were encouraging, complete, permanent relief from pain being obtained in many cases, while in the majority of the remainder there was long-lasting improvement. In this paper he analyses the results in 282 of these cases. He first stresses the social importance of rheumatic conditions, which affect 5% of the population of the United States, and cites a statement from a U.S. Government survey published in 1936 to the effect that "rheumatism ranks first in prevalence, second in causing chronic disability, second in causing invalidity (permanent disablement), and only fourteenth in causing death". He then reviews the treatment of these conditions by cortisone, ACTH, and pregnenolone, and points to the disadvantages of these preparations. They often have only a temporary effect, and their administration may lead to physiological or psychical disturbances. He briefly touches on gold therapy, and mentions the difficulty of distinguishing the borderline between the therapeutic and the toxic dose.

The radiotherapy of arthritis was first introduced by Sokolov in 1897; although it was not much used in the U.S.A. until 1933, it was extensively employed in Europe. The author quotes the good results obtained with x rays by other workers in cases of spondylitis, especially those of Marie-Strümpell type. He considers early treatment to be essential, and states that his best results were obtained when radiotherapy was combined with breathing and postural exercises. The strength of the current was varied according to the size of the joint to be irradiated, a medium voltage being used for small joints and a high voltage for larger ones. In the acute stage 3 treatments a week for 2 to 3 weeks were given, followed by one treatment weekly for another 5 or 6 weeks. In chronic cases 1 to 2 treatments were given weekly for several weeks. The author found that arthritis of rheumatic origin required a higher voltage and heavier filtration, than other conditions.

The most commonly occurring bursitis was that of the subdeltoid bursa; bursitis affecting the olecranon or knee and prepatellar bursitis came next in frequency. The author mentions other conditions of the shoulder which may simulate bursitis, and warns that neglected bursitis may lead to "frozen shoulder". He also refers to brachial neuralgia and points out that this can easily be differentiated from bursitis because in the former, but not in the latter, neuralgia causes pain while the arm is at rest.

Radiotherapy should be continued until complete mobility of the joint is restored; this usually requires 8 to 10 sessions of 100 r each at 180 kVp, with a filter of 0.5 mm. Cu and 1 mm. Al and a focus-skin distance of 50 cm. Acute and subacute cases responded rapidly; in chronic cases a dose of 1,000 r was often necessary to relieve pain and to restore mobility. Improvement was steady though slow.

The author discusses the aetiology of radiculitis, and concludes that this condition may be caused by any disease, toxic absorption, or mechanical factor which irritates the intraspinal or paraspinal elements. The main feature of radiculitis is pain of typical segmental distribution or arising in areas innervated by the affected nerve root. Involvement of a motor nerve root results in muscular weakness, atrophy, and electrical changes. In brachial-plexus radiculitis, which is often associated with bursitis and arthritis, the author recommends a dose of 1,200 r. He also describes the dorsal-spine radiculitis syndrome. The possibility of the coexistence of radiculitis and coronary pain is pointed out. Segmental pain of the abdominal wall, the author states, may simulate lesions of the gastro-intestinal or genitourinary system.

In discussing sciatica the author considers only those cases which are due to arthritis. Radiotherapy in these cases proved to be most beneficial. He employed a high-voltage current with 0.5 mm. Cu and 1 mm. Al filtration, an average of 1,500 r being given. A 15-cm. cone was used to localize the irradiation. In the lumbo-sacral area great care should be exercised in both sexes and a dose of 600 r never exceeded. The author considers that in these cases his results were satisfactory.

In giving x-ray treatment for rheumatic conditions

great care must be taken of the skin, as it is hypersensitive over affected areas. Any reaction calls for curtailment or postponement of the treatment. A protective ointment containing antihistaminic drugs was used with good results.

Seven interesting tables have been included, and these enable results to be appreciated at a glance.

L. G. Capra

See also Pathology, Abstract 1870,

RADIODIAGNOSIS

1845. Roentgenologic Demonstration of the Facial Nerve Canal

M. J. TAMARI and A. LOEWY. *Archives of Otolaryngology* [Arch. Otolaryng., Chicago] 53, 34-40, Jan., 1951. 8 figs.

By a special technique it is possible to demonstrate the course of the facial canal, except through the dense labyrinthine block, in compact or pneumatic mastoids. In the compact bone the canal can usually be shown by increasing the penetration when making the exposure. Three positions are employed: the Stenver, the modified Chamberlain-Towne, and the Schüller-Law. The canal is best seen in the Schüller-Law view, but the facial area in the internal auditory meatus is often distinct in Stenver's view, and the region of the stylomastoid foramen is well shown in the modified Chamberlain-Towne position.

Erosion by cholesteatoma or carcinoma was revealed radiologically and confirmed at operation. It was also possible to demonstrate radiologically abnormalities in the course and in the size of the facial canal. A very interesting point is that in a small series of patients with a history of previous Bell's palsy an unusually narrow canal was demonstrated; this observation, if consistently repeated, would support the theory of a vascular cause for idiopathic facial palsy.

F. W. Watkyn-Thomas

1846. Air Cells in the Great Wing of the Sphenoid Bone
R. WIGH. *American Journal of Roentgenology and Radium Therapy* [Amer. J. Roentgenol.] 65, 916-923, June, 1951. 11 figs., 1 ref.

The primary purpose of this study is to describe a variation in the pneumatization of the sphenoid bone consisting of an accessory nasal-sinus compartment in the vertical plate of its great wing. This occurs in about 1% of cases and may be bilateral. The recognition of this normal variant is important, as otherwise a destructive process of bone may be suspected.

The air cell in the perpendicular plate of the sphenoid wing appears in the frontal projection as a central radio-translucency surrounded by a well-defined sclerotic margin. The superior and lateral walls are readily traced, but the inferior portion of the recess is concealed by the density of the petrous pyramid. Even Waters's projection will usually fail to reveal a lower boundary, because the air compartment does not end in the orbital

plate of the bone, but continues by curving posteriorly into the floor of the middle fossa.

The appearances may be occasionally simulated by other conditions; thus, a well-defined transverse venous sinus superimposed on the great wing may produce a rather similar pattern. A very thin wing will be radio-translucent, particularly centrally, and this may very closely simulate an air cell. However, the margin is not so distinct and a Waters projection will indicate that the translucency is entirely above the foramen rotundum and not continuous with an air cell below in the horizontal plate. Occasionally air cells are found in the superior part of the great wing with unpneumatized bone beneath them; their continuity with the ethmo-frontal cells will, however, be obvious.

Further corroboration that one is dealing with a variant associated with exceptional pneumatization of the phenoid bone rather than with a destructive process is obtained from the base view. Invariably the sphenoid sinus will be seen to be very large, and should have recesses which extend laterally beyond the foramen ovale and the anticipated position of the foramen spinosum.

L. G. Blair

1847. Bronchography in Tuberculosis. (Bronchographie bei Tuberkulose)

G. IBERS, H. VIETEN, and K. H. WILLMANN. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [Fortschr. Röntgenstr.] 74, 667-676, June, 1951. 9 figs., bibliography.

The authors discuss the value of spot-film bronchography with water-soluble, viscous "perabrodil M" 60%. No ill effects were observed; in particular there was no activation of the tuberculous process and no bronchogenic or haematogenic spread of the infection. Nevertheless the authors believe that the method should be employed only in those cases where all other methods of investigation have failed to locate tuberculous bronchial changes, bronchiectasis, and bronchostenosis; the method is also useful for checking the results of thoracoplasty.

A. Orley

1848. Clinical and Experimental Studies in the Use of a Water-soluble Agent for Bronchography

M. E. PECK, A. J. NEERKEN, and E. SALZMAN. *Surgery, Gynecology and Obstetrics* [Surg. Gynec. Obstet.] 92, 685-692, June, 1951. 17 figs., 18 refs.

The authors review the disadvantages of "lipiodol" as an agent for bronchography. These are related to its retention in the alveoli and the dangers associated with reactions to the injected material. The Swedish work on "umbradil" made up in an aqueous solution of sodium carboxymethyl cellulose, and the Swiss work with glycolmethyl cellulose as a base, are noted.

The authors have used diodone in association with pectin, but found that on account of its low pH there was a tendency to liberate free iodine. Following on the studies of pure methylcellulose as a blood substitute during the war of 1939-45, they used a 1.75% solution of this substance in 50% diodone. Details of the process are given. Initial experiments were carried out

upon guinea-pigs. The material was injected intratracheally and the animals were killed after intervals of 3 hours to 4 weeks. No abnormality was found at necropsy beyond an occasional small area of focal atelectasis. Subsequent experiments were carried out on dogs, in which a high incidence of bronchopneumonia was found; but as there was a similar occurrence after the use of iodochloral it was felt safe to proceed with a clinical investigation. No allergic reactions have as yet been observed. A skin sensitivity test was carried out before the injection. The authors report that the material tends to adhere to the bronchial mucosa, resulting in a mucosal relief picture. It mixes readily with bronchial secretions, so that partially filled bronchiectatic areas are outlined. Droplet formation does not occur. They consider that radiographs should be taken within 2 to 3 minutes after instillation, and experienced no difficulty in this respect. Three illustrative cases, are described.

John H. L. Conway-Hughes

1849. Solitary Pulmonary Necrosis. A Comparison of Neoplastic and Inflammatory Conditions

R. WIGH and F. R. GILMORE. *Radiology* [Radiology] 56, 708-718, May, 1951. 8 figs., 21 refs.

The use of the new chemotherapeutic agents has brought about a change in the relative importance of neoplasms and of infection in the causation of solitary pulmonary necrosis. In the past, abscess formation was a common sequel of infection and the majority of non-tuberculous cavities were caused in this way. This is no longer the case; among the cases seen at the Jefferson Medical College Hospital between 1946 and 1950, 19 were of inflammatory origin and 18 neoplastic. A non-tuberculous, single cavity in a patient of 40 years of age is more likely to be due to neoplasm than to infection.

Films of the 37 cases concerned were reviewed with the object of establishing points of distinction between the two forms of abscess. Five of the neoplastic cavities occurred in atelectatic segments distal to an obstructing endobronchial growth; the tumour was visible on bronchoscopy in most of these cases. In any event, the presence of segmental atelectasis should give the diagnosis, for this condition occurs to a minor extent, if at all, in benign abscesses. In the larger group of cases the cavity forms within a peripheral type of pulmonary neoplasm, and these are often very difficult to distinguish from simple abscesses. Helpful points in diagnosis are the presence around the cavity of a tumour that is more circumscribed and clearly defined than the inflammatory zone round an abscess. Sometimes such a mass is seen to cross, or bulge into, an interlobar fissure; this is diagnostic of neoplasm. Malignant cavities usually have better-defined but less regular walls and tend to occur in the centre of the tumour mass, while inflammatory abscesses are more smoothly rounded and are often eccentrically placed.

J. A. Shiers

1850. Selective Angiocardiography. (Cardioangiografia selettiva)

G. TORI. *Annali de Radiologia Diagnostica* [Ann. Radiol. diagnost.] 23, 280-294, 1951. 16 figs., 12 refs.

1851. Enlarged Gastric Rugae: a Correlation of the Roentgenologic, Gastroscopic, Pathologic, and Clinical Findings. Analysis of Forty-one Cases

W. W. VAUGHAN, J. U. GUNTER, and E. A. ERWIN. *Radiology* [Radiology] 56, 813-831, June, 1951. 18 figs., 7 refs.

For this study 41 patients with coarse gastric rugae were selected from over 20,000 patients who had been subjected to more than 30,000 barium-meal examinations between 1940 and 1950. The grounds for selection were repeated x-ray examinations, gastroscopy, and full investigation. The average width of the rugae was 8 mm.

Ulcer-like symptoms occurred in 14 out of the 41; the remainder complained of epigastric distress, vomiting, nausea, and loss of appetite. There was a history of haemorrhage in 12, and in one case the bleeding was massive. A histamine test-meal examination was carried out on 38 patients; 12 showed no free hydrochloric acid on two or more examinations, 8 had hypoacidity, and 10 hyperacidity. Gastroscopy revealed enlargement of the folds with some loss of flexibility; nodulation, producing a cobble-stone appearance, was common; the colour of the mucosa ranged from a beefy red to a yellowish grey; and superficial ulceration with bleeding was present in 8 cases.

Subtotal gastric resection was performed in 4 cases; and in 4 tissue was removed for biopsy. The histology was difficult to interpret. Lymphocytes and plasma cells in the mucosa were regarded as normal, but excessive numbers of lymph follicles and inflammatory cells in the submucosa were considered significant. The authors conclude that chronic enlargement of the gastric rugae is indicative of either a chronic gastritis or neoplastic infiltration.

[As with so many American statistical papers, it is impossible to reconstitute the individual cases. No attempt is made to distinguish between the "pyloric syndrome", with massive acid eructations, and true vomiting. Thickening of the gastric folds is frequently seen in association with the hyperaemia of hypersecretion. Rigid, thick folds associated with histamine achlorhydria are relatively uncommon, and the more likely diagnosis is generalized chronic gastritis.]

Denys Jennings

1852. The Radiological Signs of Congenital Hypertrophic Pyloric Stenosis and their Regression after Operation. (L'évolution radiologique des signes de sténose du pylore opérée chez le nourrisson)

C. PROUX and J. A. HUMMEL. *Semaine des Hôpitaux de Paris* [Sem. Hôp. Paris.] 27, 1603-1606, May 18, 1951. 7 figs.

The authors observe that certain clinicians doubt the usefulness of radiological examination in congenital hypertrophic pyloric stenosis and rely on the clinical picture; they point out that the clinical picture is often incomplete, and a clinical assumption can be turned into a certainty by radiological examination. Their technique is described. This involves starving the infant for 8 or 9 hours and spreading the examination over 5 hours. The radiological signs on which they base their diagnosis

are: retention of fluid in the stomach, through which the barium falls like snow; dilatation of the lower end of the stomach; altered peristalsis (the stomach passes from atony to spasm, peristaltic waves start high up on the greater curvature and are deep and slow); obstruction to the flow of barium at the pylorus is not usually complete; there is almost invariably a residue between 5 and 24 hours. The pyloric antrum has a "double-cup" appearance which, with the prominent duodenal bulb, outlines the tumour. The pyloric canal is elongated but not always narrowed.

The authors state that the regression of radiological signs following operation is dependent on time; at first the appearances are unchanged. They believe that the stenosis is undoubtedly due to muscular hypertrophy associated with considerable spasm.

John H. L. Conway-Hughes

1853. Subcutaneous Urography: Description of a New Method utilizing 70% Urokon and Hyaluronidase. A Preliminary Report

J. E. BYRNE and W. F. MELICK. *Urologic and Cutaneous Review [Urol. cutan. Rev.]* 55, 193-199, April, 1951. 13 figs., 15 refs.

The method of subcutaneous or intramuscular pyelography is very useful in infants, where pyelography by the intravenous route is fraught with great difficulty. This paper evaluates a method whereby a 70% solution of "urokon" (a new organic iodide) is given subcutaneously with hyaluronidase to improve absorption.

The effect of local injection was first investigated on guinea-pigs, the sites of injection being studied microscopically after 24 hours. Local tissue reaction or necrosis was not seen after urokon, but was present to a marked degree after injection of 90% sodium iodide or 70% diodone. Urography was then carried out on 25 normal infants. An ampoule of commercial hyaluronidase was diluted to 2 ml., and 1 ml. injected into each thigh: 0.5 g. of urokon per kg. body weight was then injected into these sites. As soon as a kidney shadow was seen a feed of milk was given, as a stomach filled with milk serves as a "radiographic window" for visualization of the kidneys. The average time of appearance of the dye in the kidneys with this technique was 45 minutes. The pyelograms were considered satisfactory.

F. B. Cockett

1854. On the Evaluation of the State and Function of the Deep Veins of the Limbs: Technique of Intra-osseous Phlebography. (К вопросу оценки состояния и функции глубоких вен конечностей)

V. N. SCHEINIS. *Хирургия [Khirurgiya]* No. 5, 23-29, May, 1951. 2 figs.

This is a very interesting account of experimental intra-osseous phlebography [for phlebographia perosteomedullaris transosteomedullaris, as the author prefers to call it] of deep veins performed on 27 rabbits. The radio-opaque solution (a Soviet product called "sergosin") was injected into the os calcis (the injection being as easy and rapid as intravenous injection) and the exposure made immediately on completing the injection.

Mention is also made of a few very satisfactory trials in patients. [The article is a useful contribution to the subject of phlebography.]

Nicolas Tereshchenko

1855. Pneumo-arteriography. (La pneumoarteriografia)
G. D'ERRICO and L. PISCITELLI. *Giornale Italiano di Chirurgia [G. ital. Chir.]* 7, 307-317, May, 1951. 7 figs., 6 refs.

Accidents and complications attendant upon the use of contrast media in arteriography have fortunately become less frequent than in the past, but they have not yet been entirely eliminated. The use of contrast media, which till now have been confined to thorium dioxide and iodine-containing compounds, has the disadvantage of producing neoplastic reactions in the reticulo-endothelial system, pain, or irritation of the endothelial lining. The authors therefore set out to find a medium which would not produce any side-effects and would be completely absorbed very shortly after injection into the blood stream. With this in view they decided to try injections of oxygen into the arterial tree. Preliminary animal experiments showed that it was possible to inject a comparatively large quantity (up to 70 ml. in 2 to 3 seconds) of oxygen without producing any reaction either at the time of administration or subsequently.

Their technique in human beings consists in introducing a small needle (No. 14) into the artery and then injecting from 35 to 70 ml. of oxygen by means of a two-way syringe large enough to hold the desired quantity of gas. The femoral artery was punctured in Scarpa's triangle, and once the operator had made certain that the needle was in the artery the injection was carried out in 2 to 3 seconds. (The authors have experimented with blocking the circulation by manual pressure over the iliac artery.) A radiograph was taken towards the end of the injection when it was desired to outline the arteries of the thigh, and for those of the lower leg the radiograph was taken a moment or two later, very soft x rays being used and the exposure varying from 0.2 to 1.5 seconds. The focal distance depended on the area of the limb and the segment of artery to be examined. Usually a focal distance of 100 cm. was found to be adequate. Clearer pictures could be obtained by using a rotating anode and a Potter-Bucky diaphragm.

The authors have used this method with great success in cases of gangrene and of endarteritis obliterans. The method was also employed successfully in a case of arteriovenous aneurysm, in which the injection was given direct into the aneurysmal sac. As the oxygen was rapidly absorbed by the blood, no embolus or other complication occurred. Other advantages are that the examination can be carried out on the ambulant patient and no anaesthetic or analgesic is necessary. The method is not costly, and the authors claim that the results are comparable to those obtained by the use of opaque media.

The authors have also made various attempts to use oxygen for phlebography, either by direct injection into the vein or by endosteal administration, but the results have not been satisfactory.

J. Rabinowitch

Pathology

EXPERIMENTAL

1856. Studies on Cross Circulation in Man. I. Methods and Clinical Changes

H. R. BIERMAN, R. L. BYRON, K. H. KELLY, K. S. DOD, and P. M. BLACK. *Blood [Blood]* 6, 487-503, June, 1951. 11 figs., 20 refs.

The authors report their experiences in 7 cross-transfusions in human beings. They used this method to investigate the pulmonary leucocyte removal mechanism previously reported by one of them. Two transfusions were made by vein-to-vein, 1 by artery-to-vein, and 4 by artery-to-artery connexion. This last procedure does not require any artificial pumping mechanism. Full details of the technique for setting up the artery-to-artery connexions are given. Patients were kept heparinized throughout the transfusion, but in one case arterial embolism occurred with resultant dry gangrene. For this reason in the last experiment all apparatus was siliconed. In 5 cases blood from a leukaemic subject was exchanged with that of a patient suffering from malignant disease, in another both subjects had leukaemia, and in yet another 1 patient had Hodgkin's disease, the other carcinoma of the testis. The duration of the transfusions varied from 2 to 26 hours, resulting in from 900 ml. to 150 litres being exchanged.

In the first 3 transfusions the same leukaemic patient was transfused from 2 different partners. On each occasion the leucocyte count of the leukaemic child fell most markedly after the termination of the exchange. In the fourth transfusion a marked fall in the patient's leucocyte count occurred during the exchange, this patient showing considerable diminution of mediastinal infiltration. In the fifth cross-transfusion there was no change in the leucopenia of the patient with Hodgkin's disease despite a fall in his partner's leucocyte count. In the sixth exchange, between 2 patients with leukaemia (1 myeloid and 1 aleukaemic lymphatic), there was equilibration of the leucocyte counts with the appearance of many myeloid cells in the blood of the patient with lymphatic leukaemia. In the seventh and longest transfusion the aleukaemic patient's leucocyte count rose and his partner's fell, but there remained a difference of 1,500 cells per c.mm.

In all cases the counts returned to the pre-transfusion level. One of the patients with leukaemia is still alive, his condition being unchanged. All the patients with malignant disease have died, but no evidence of leukaemic infiltration was found at necropsy. Apart from the case of arterial embolism surprisingly few complications have occurred. It is suggested that in some leukaemias a failure of the leucocyte removal mechanism exists, and the exchange in which 2 leukaemic patients were partners is further evidence for this theory. The authors conclude by discussing fully the hazards of this procedure, but

believe that the technique will prove of value in the investigation of the formed elements and the chemical constituents of the blood.

R. F. Jennison

1857. Hypertensive Cardiovascular Disease. Vascular Lesions of Dogs Maintained for Extended Periods following Bilateral Nephrectomy or Ureteral Ligation

E. E. MUIRHEAD, L. B. TURNER, and A. GROLLMAN. *Archives of Pathology [Arch. Path., Chicago]* 51, 575-592, June, 1951. 9 figs., 10 refs.

The pathological changes originally observed in dogs after bilateral nephrectomy were those of "malignant" hypertension. If, however, the animals can be kept alive for more than 10 days, by the use of peritoneal lavage and a low salt diet, the lesions come to resemble those of "benign" hypertension.

From a study of 32 animals, of which 22 underwent bilateral nephrectomy and 10 ligation of the ureters, it is apparent that the pathological changes can be divided into three groups, which are roughly proportional to the length of survival. Hyperacute lesions consisting of medial necrosis of arterioles are present in animals living less than 10 days after operation; acute changes, medial necrosis with early hyaline degeneration, are seen in dogs which survive for 10 to 20 days; while in those surviving for longer periods total hyalinization of the vessel wall occurs in an eccentric manner with displacement of the lumen to one side, or thickening and increased cellularity of the arteriole due to fibrous proliferation. These subacute and chronic changes are also accompanied by subendothelial proliferation and increase in the internal elastic lamina. Lesions corresponding to these three grades are also found in the heart muscle. The arteriolar involvement is especially marked in the vessels of the intestinal tract and is notably absent only in those of the pulmonary circulation.

All animals surviving more than 10 days after nephrectomy develop marked hypertension, but little or no increase in blood pressure occurs in those undergoing ligation of the ureters. Nevertheless, some of the latter animals develop severe arteriolar lesions, and this, with the lack of correlation between the degree of hypertension and the pathological changes in the nephrectomy group, seems to indicate that hypertension *per se* is not the factor responsible for these changes.

A. Paton

1858. Sustained Hypertension following the Administration of Desoxycorticosterone Acetate

S. M. FRIEDMAN, C. L. FRIEDMAN, and M. NAKASHIMA. *Journal of Experimental Medicine [J. exp. Med.]* 93, 361-371, April 1, 1951. 1 fig., 18 refs.

Pellets containing approximately 25 mg. of desoxycortone acetate (DCA) were implanted subcutaneously into a number of normal, intact male rats. In the first experiment 53 animals received DCA on the 6th

and 8th days; 1% salt solution was substituted for drinking water 1 week after treatment began. Two weeks after treatment began the pellets were removed and the animals again given water to drink for 2 weeks. The second course was like the first; the third lasted 1 week longer. The 47 surviving animals, with 21 controls, were then observed for 54 weeks; of 15 survivors, 7 were never hypertensive, 4 were occasionally hypertensive, and 4 were definitely hypertensive.

In the second experiment 40 animals received pellets on the 5th, 11th, 15th, 25th, and 29th days and 1% saline instead of drinking water from the 4th to the 19th day. At 40 days the pellets were removed and the 31 survivors observed for 54 weeks; 24 animals survived for a significant period, and of these 11 were not hypertensive, 6 were occasionally hypertensive, and 7 definitely hypertensive. In both experiments the blood urea level showed no significant variations. Just after the minimal DCA treatment in the first experiment the kidneys showed few significant changes at all. Later, there was only minimal glomerulosclerosis and no tubular damage, the main lesion being a medial hypertrophy of the smaller arteries and arterioles amounting almost to obliteration of the lumen and with numerous areas of focal infarction. After the second experiment there was some glomerular sclerosis and some focal tubular damage, with dilatation and casts. There were some parenchymal scars. There did not appear to be any difference between the kidneys of the hypertensive and the normotensive animals.

The authors consider that the anatomical changes in the kidneys do not account for the increase in blood pressure, and therefore that the condition in rats bears some relation to benign hypertension in man. They suggest that the adrenal cortex produces a pressor agent which is normally eliminated by the kidney, and that impairment of this function leads to a raised blood pressure.

Peter Harvey

1859. The Effect of Removing the Constriction of the Renal Artery in Acute and Chronic Hypertension in the Rabbit

R. B. BLACKET and A. L. SELLERS. *Clinical Science [Clin. Sci.]* 10, 177-183, 1951. 2 figs., 16 refs.

Hypertension in the rabbit can be produced by clamping one renal artery, the opposite kidney having previously been removed. It has been shown that during the first week after clamping of the renal artery the rise in blood pressure is due to the release of a humoral agent, probably renin, from the ischaemic kidney. In this paper is described the experimental investigation of the factors operating in the maintenance of prolonged or chronic hypertension in the rabbit.

Unilateral nephrectomy and clamping of the renal artery of the remaining kidney were performed in 10 rabbits, as a result of which hypertension developed in all of them. The animals were then divided into two groups. In one group, of 4 animals, the clamp was removed 2 to 17 days after its application, and as a result the blood pressure in 3 rabbits returned to normal within 24 hours; in the fourth the greatest fall in blood pressure occurred during this period, but there was a slight further reduction

up to about the 6th day. In the 6 rabbits of the second group the clamp was removed 6 to 24 weeks after its application. In 2 of these the blood pressure became normal in 24 hours, whereas in the remaining 4 it took from 4 to 23 days to reach the basal level.

The authors claim that these experiments confirm the previous finding that in the early stage of hypertension following constriction of the renal artery raised arterial pressure is due solely or chiefly to the release of renin by the ischaemic kidney. It would appear that in the later stages (chronic hypertension) the ischaemic kidney is also the main factor in maintaining the raised arterial pressure. This could, theoretically, be achieved in two ways. (1) A substance normally excreted by the kidney could accumulate in the body during renal ischaemia or insufficiency and lead to hypertension by changing the chemical composition of the body; this substance would be excreted gradually after unclamping. (2) The secretion of a depressor substance normally elaborated by the kidney could be deficient during prolonged renal ischaemia and gradually reappear in the blood after the clamp is removed. In addition, the function of other organs or endocrine glands could be affected by the chemical changes in the body during renal ischaemia in such a way that hypertension results.

A. I. Suchett-Kaye

1860. Oedema and Capillary Anoxia

R. C. NAIRN. *Journal of Pathology and Bacteriology [J. Path. Bact.]* 63, 213-234, April, 1951. 3 figs., bibliography.

Dogs were perfused with deoxygenated blood under conditions as nearly physiological as possible. This perfusion was carried out by passing blood from the femoral vein of one hind limb (the donor limb) through the femoral artery of the other hind limb, the pressure of the venous blood delivered to the perfused artery being increased to arterial level by means of a perfusion pump. After supplying the perfused limb, the twice-used blood returned by the femoral vein of that limb to the heart for natural recirculation through the body of the animal. The dogs were under pentobarbitone or thiopentone and ether after premedication with atropine. Five experiments were carried out. At no time was oedema found in the perfused limb or elsewhere. The percentage of water in the muscles after death was the same in all limbs. This finding is considered valid, the author showing that possible disturbing factors such as alterations in venous pressure and capillary permeability and protein transfer could be excluded.

In order to determine whether capillary anoxia could aggravate oedema caused by other agents 4 experiments were performed in which generalized oedema was produced by intravenous administration of saline during perfusion experiments. The results were negative. Acute hypoproteinaemia was produced in 1 dog by several plasmaphereses, the final protein level being 1.7 g. per 100 ml. Ascites and generalized oedema developed, but the water content of the perfused and control limbs remained the same.

In 4 experiments venous congestion was produced by

inflatable cuffs. Oedema developed in proportion to the increase in venous pressure above 23 cm. saline, but was not more in the perfused limb than in the control. Similarly the rate of absorption of local depots of fluid consisting of normal saline injected subcutaneously, of normal dog serum injected intradermally, and of the local oedema of serum sensitivity was unaffected by capillary anoxia.

It was also established that the experimental conditions had no inhibitory effect on the production of oedema: the wheals of intradermal horse serum in a sensitized dog developed at the same rate, reached the same size, and were absorbed at the same rate, both before and after atropine, pentobarbitone, and heparin administration, as during a standard perfusion experiment. Nor was increased lymphatic drainage a factor which might have been responsible for failure to develop oedema in the perfused limb.

The author therefore concludes that capillary anoxia plays no part in the production of oedema.

R. B. Lucas

1861. Sustained Hyperlipemia Induced in Rabbits by means of Intravenously Injected Surface-active Agents

A. KELLNER, J. W. CORRELL, and A. T. LADD. *Journal of Experimental Medicine* [J. exp. Med.] 93, 373-383, April 1, 1951. 2 figs., 27 refs.

In a 0.9% saline solution, buffered with McIlvaine's solution to pH 7.3, a 20% solution of "tween 80" or 12.5% solution of commercial "triton A 20" was intravenously injected into rabbits. All animals were fed on a cholesterol-free diet. The initial injections caused some transient toxic manifestations.

A single intravenous injection of the optimal dose (2.5 mg. per kg.) of tween 80 in 6 rabbits caused a rise in blood cholesterol level of 46 to 260% and in that of phospholipids of 111 to 338% in 6 to 12 hours, returning to normal in from 24 to 48 hours. Twelve rabbits received optimal doses of tween 80; 24 hours after the first injection further injections were given every 8 hours, totalling 8 to 31 doses. The blood level of cholesterol increased to 335 to 1,030 mg. per 100 ml. and that of phospholipids to 370 to 1,050 mg. per 100 ml. The rise and fall were parallel, with slightly higher phospholipid levels. When the injections were stopped levels returned to normal in 5 to 8 days. Four animals died during the experiment, and in 4 rabbits the levels had not entirely returned to normal in 6 to 10 days.

Six rabbits each received a single injection of 2.5 ml. of triton A 20 per kg. The blood cholesterol level rose to 244 to 255 mg. per 100 ml. and the phospholipid level to 358 to 1,240 mg. per 100 ml. Peaks were reached in 1 to 3 days, and phospholipid levels were higher than cholesterol levels. Normal levels were reached again after 5 to 15 days.

At 24 to 48 hours after the injections there was a much greater increase in concentration of free than of esterified cholesterol and the total lipid content was much higher than those of cholesterol and phospholipid, so that the neutral-fat content was raised as well. When

4 ml. of triton A 20 was given intravenously to rabbits twice weekly for 9 weeks there was a progressive increase in cholesterol and phospholipid levels, which in some cases exceeded 2,000 mg. per 100 ml. blood.

The authors point out that this form of hyperlipaemia differs from that resulting from cholesterol feeding. There seems to be little evidence, but much speculation, as to the mechanism by which this is brought about.

Peter Harvey

1862. The Influence of Intravenously Administered Surface-active Agents on the Development of Experimental Atherosclerosis in Rabbits

A. KELLNER, J. W. CORRELL, and A. T. LADD. *Journal of Experimental Medicine* [J. exp. Med.] 93, 385-398, April 1, 1951. 23 refs.

In this investigation rabbits were fed on a cholesterol-free diet and various added substances were put in their feeding-cups on alternate days. The first experiment lasted 13 weeks. In Group 1 (control) 7 rabbits were fed on a normal diet to which 0.5 g. of cholesterol was added. Group 2 consisted of 5 rabbits on a normal diet with in addition 7.5 ml. of 20% "tween 80" intravenously twice daily; the 6 rabbits in Group 3 received both cholesterol and tween 80.

In Group 1 there was moderate elevation of the serum cholesterol and phospholipid levels, the former being higher than the latter; 5 of the 7 animals developed atheroma. In Group 2 pronounced hyperlipaemia was present and the phospholipid levels were higher than the cholesterol levels. None of the 5 rabbits showed atheroma. In Group 3 there was considerable lipaemia, the phospholipid level being higher than the cholesterol level. The sole survivor showed only slight atheroma.

In the second experiment, Group 4 consisted of 11 animals given 1.0 g. of cholesterol and 10 ml. of tween 80 with their diet. There was marked elevation of their blood cholesterol and phospholipid levels, the cholesterol level being the higher; all had atheroma at necropsy, pronounced in 5 cases. In Group 5 were 11 rabbits which received twice weekly an intravenous injection of 4 ml. of 12.5% "triton A 20". The serum lipid levels were similar to those in Group 4, but the phospholipid levels were higher than the cholesterol levels; 6 of the animals showed no atheroma, but 4 had slight and 1 extensive lesions. Group 6 was composed of 11 animals given 0.5 g. of cholesterol and 4.0 ml. of tween 80 with their diet. In Group 7 were 8 animals given 1 g. of cholesterol and 10.0 ml. of tween 80 with their diet. Animals in Groups 6 and 7 received intravenous injections similar to those given in Group 5. Both groups showed sustained elevation of the cholesterol level above that in Group 4, and the phospholipid level, though elevated, was considerably lower than the cholesterol level; 7 animals showed no atheroma and 12 had minor lesions. The lesion which occurred in Group 5 is the first to be produced experimentally without the introduction of exogenous cholesterol.

In the third experiment 23 rabbits received 1.0 g. of cholesterol and 10.0 ml. of tween 80 added to their diet for 8 weeks. Then 7 of them were killed and the 16

surviving animals were maintained on the stock diet for a further 8 weeks. Thereafter 8 animals received 7.5 ml. of 20% tween 80 twice daily for 8 weeks; all were then killed. No significant difference was found between this group and the last two groups.

The authors suggest that their experiments support the hypothesis that a low serum phospholipid level in relation to the serum cholesterol level, by altering the colloid stability of the lipid emulsion, may be one of the factors involved in the pathogenesis of atheroma.

Peter Harvey

1863. Significance of Endogenous Cholesterol in Arteriosclerosis: Synthesis in Arterial Tissue

M. D. SIPERSTEIN, I. L. CHAIKOFF, and S. S. CHERNICK. *Science [Science]* **113**, 747-749, June 29, 1951. 12 refs.

The aortas of 3 chickens and 2 rabbits were cut into sections about 0.5 cm. long and incubated for 3 hours at 37.5° C. in Krebs's bicarbonate buffer solution containing 1 g. of acetate doubly labelled with radio-active carbon (¹⁴C) by the method of Barker *et al.* The carbon dioxide evolved was trapped in caustic potash and its ¹⁴C content determined. The tissue was then hydrolysed with 90% caustic potash and 95% alcohol for 6 to 12 hours, precipitated, and the cholesterol extracted. It was found that the aortas of rabbits and chickens converted considerable quantities of acetate to carbon dioxide and synthesized small quantities of cholesterol. Liver slices synthesized cholesterol four times as quickly as the aortic slices. The findings indicate that endogenous cholesterol, originating probably in the artery, may be of greater importance in the pathogenesis of spontaneous arteriosclerosis than has hitherto been supposed.

H. E. Holling

1864. Effect of Transplantation of Antrum of Stomach on Gastric Secretion in Experimental Animals

L. R. DRAGSTEDT, E. R. WOODWARD, H. A. OBERHELMAN, E. H. STORER, and C. A. SMITH. *American Journal of Physiology [Amer. J. Physiol.]* **165**, 386-398, May 1, 1951. 7 figs., 7 refs.

The object of the authors' experiments was to demonstrate in dogs the influence of the pyloric antrum on the acid secretion of the remainder of the stomach. In a previous paper the authors showed that the total removal of the antrum profoundly reduced the acid secretion of Pavlov-pouch preparations, whereas removal of two-thirds had no effect. They now describe experiments in which they have succeeded in isolating the pyloric antrum from the remainder of the stomach, draining it through the abdominal wall or reimplanting it into another viscus.

These experiments were designed to determine whether the antral mechanism of stimulating the gastric secretion is entirely hormonal or partially mediated through a local nerve-plexus reflex. In 4 animals the stomach was totally isolated from the remainder of the alimentary tract and its secretions collected externally. The duodenum was anastomosed to the oesophagus and the vagi divided. Only a small amount of acid was

secreted daily in the next few weeks. At a second operation the antrum was isolated from the body of the stomach, but the separation posteriorly was of mucosa only, leaving a sero-muscular bridge connecting the two. The antral pouch was implanted into the duodenum, allowing free entrance of intestinal contents into it. After this procedure the acid secretion was increased 15 times. At yet a third operation the seromuscular bridge was divided. This had no effect on secretion. This procedure was repeated in another group of animals, in which the vagi were not divided. Total stomach preparations with the vagal stimulus to acid secretion preserved secreted eight times as much as the previous group in which the vagi had been sectioned. When the antrum was separated and implanted into the duodenum, acid secretion increased four times.

In another experiment the effect of transplanting the antral pouch into the colon was investigated. This caused an increase of acid secretion twice as great as duodenal implantation. When the antral pouch was removed from the colon and its secretions drained exteriorly, the acid production fell to the control level. Finally it was implanted into the duodenum, after which secretion rose to a level comparable with that attained in the previous experiment. Pavlov pouches were prepared in another group of dogs. After a control period the pyloric antrum was separated and drained exteriorly. This lowered the acid secretion in the pouch by half. When the antrum was implanted into the colon the secretion rose to twice the control figure. In order to demonstrate the specificity of the antrum in producing these effects total stomach pouches were isolated, but instead of the antrum being separated, a pouch of fundus was made and implanted into the duodenum. No change in secretion occurred.

The factors influencing the gastric secretion of acid can be divided into vagal, antral, and residual or intestinal. The last experiment of this series was designed to elucidate the relative values of each. A total stomach pouch was prepared and the secretion collected externally. Then the vagi were divided in the chest, leaving only the intestinal factor active. Finally the antrum was isolated and implanted into the duodenum. The results showed that the intestinal factor had least effect, the vagus slightly more, and the antrum about twice the latter. All these factors acting together caused a greater secretion than the sum of the individual effects.

[This is an interesting paper. The number of animals used in each experiment was small and the results will need confirmation. All figures quoted are approximations of those given by the authors.]

A. G. Parks

1865. Alloxan Administration in the Guinea Pig. A Study of the Regenerative Phase in the Islands of Langerhans

D. D. JOHNSON. *Endocrinology [Endocrinology]* **47**, 393-398, Dec., 1950. 5 figs., 21 refs.

Unlike other laboratory animals, the guinea-pig does not develop permanent diabetes after a large dose of alloxan. Most of the β cells of the pancreatic islets

degenerate within a few hours of the injection, but regeneration proceeds rapidly so that by the 4th day the islet tissue is almost completely restored; this coincides with the restoration of a normal blood sugar concentration.

Guinea-pigs were given intravenous injections of alloxan (150 to 200 mg. per kg.) and killed at intervals between 6 and 77 hours afterwards. Necrosis of the β cells was apparent 2 hours after the injection and was progressive until about the 24th hour; by the 48th hour almost all the necrotic cells had disappeared. The remaining islets appeared normal except that the β cells were enlarged and partly degranulated and that they were not separated by connective tissue from the surrounding acinar tissue.

Examination 2 days or more after the injection showed many areas of acino-insular transformation. Four types of transition cell were found: dedifferentiated acinar cells with no zymogen granules and a few small β granules; cells with zymogen at the apex and β granules at the base; cells without zymogen granules but containing both chromatophil material and β granules; and centro-acinar cells with accumulating β granules. Many of the smaller islets contained only β cells, which were arranged in typical acinar form, and others were situated at the termination of the smallest ducts. These findings suggest that the new β cells are formed by redifferentiation from acinar and duct cells. When colchicine was injected into the alloxan-treated animals the mitotic rate in both acini and islets was subnormal. Thus the new cells do not arise by cell proliferation.

Peter C. Williams

1866. Comparison of the Anabolic and Haematopoietic Effects of Vitamin B₁₂, Methionine, and Liver Extract in the Treatment of Protein Deficiency. (Comparaison des actions anabolisantes et hématopoïétiques de la vitamine B₁₂, de la méthionine et d'un extrait hépatique antipernicieux sur la réparation de l'inanition protéique) A. ASCHKENASY and P. PARIENTE. *Revue d'Hématologie* [Rev. Hémat.] 6, 166-183, 1951. 21 refs.

White Wistar rats were given a diet virtually free of protein, but with the addition of some vitamins, for about 60 days, until their weight was approximately halved, and their erythrocyte count fell to two-thirds of the normal value. They were then fed with 7% casein, and in certain groups the diet was supplemented with vitamin B₁₂, liver extract, methionine, or both vitamin B₁₂ and methionine. They were examined every 5 days and haemoglobin value, erythrocyte and leucocyte counts, and packed cell volume determined; they were killed after 40 days and changes in the weight of the organs estimated. With the addition of methionine the recovery of the loss of weight was much more complete and the restoration of blood values was much more efficient. Reticulocyte response to methionine plus vitamin B₁₂ was almost as vigorous as to liver extract, but to methionine or vitamin B₁₂ alone it was not so marked.

The authors conclude that liver extract contains a supplementary haematopoietic factor other than vitamin

B₁₂, and that there are two distinct physiological fractions in vitamin B₁₂—namely, one acting on metabolism, which can be replaced by methionine, and another purely haematopoietic.

E. Neumark

1867. The Effect of Adrenalectomy on Experimental Hypersensitiveness

L. H. CRIEP, L. D. MAYER, and O. E. LOZANO MENCHACA. *Journal of Allergy* [J. Allergy] 22, 314-329, July, 1951. 5 figs., bibliography.

The effect of adrenalectomy on experimental hypersensitiveness was studied in 57 rabbits divided into seven groups. Some animals were adrenalectomized, some received deoxycortone acetate (DCA), and some were sensitized to horse serum. Other groups were subjected to a combination of these procedures. The degree of sensitization was judged from the precipitin titre, the Arthus phenomenon, and the anaphylactic shock. Of the sensitized and adrenalectomized animals, 7 died in anaphylactic shock, whereas of those sensitized only, all survived. The Arthus phenomenon was less marked and the precipitin titres were much lower in the latter group. In the group of animals which were sensitized and also received DCA, but were not adrenalectomized, sensitization was somewhat more marked than in those which were sensitized only, but it was not as pronounced as after adrenalectomy. It is concluded that adrenalectomy enhances the reactions of hypersensitiveness.

H. Herxheimer

MORBID ANATOMY

1868. Cardiac Concentric Hypertrophy in Children with Hydrocephalus due to Tuberculous Meningitis

J. L. EMERY. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 26, 245-248, June, 1951. 6 figs., 18 refs.

A brief description is given of 6 cases out of a consecutive series of 16 children who died from tuberculous meningitis which had been treated with streptomycin. Hydrocephalus was present in each of the 6 cases. The heart weight in several cases was higher than the average normal weight, but in all cases was disproportionately high when compared with the diminished weight of the other organs. The left ventricle in each case was concentrically hypertrophied. It is suggested that the hypertrophy was due to hypertension of cerebral origin, similar to the hypertension produced in animals by medullary ischaemia and by cisternal injection of kaolin.

F. A. Langley

1869. The Embryology of Congenital Cysts of the Lungs and Bronchiectasis. (Angeborene Lungenzysten und Bronchiektasen, betrachtet vom entwicklungsgeschichtlichen Standpunkt)

O. NEYSES. *Zentralblatt für Allgemeine Pathologie und Pathologische Anatomie* [Zbl. allg. Path. path. Anat.] 87, 321-330, July 20, 1951. 3 figs., 22 refs.

The author has had the opportunity of studying, at necropsy, 2 cases of single cyst of the lung and 1 case of congenital bronchiectasis. On histological

and embryological grounds he proposes a hypothesis that cysts of the lung are due to endodermal maldevelopment, and congenital bronchiectasis to added mesodermal disturbance. The rare condition of congenital emphysema is supposed to be due to an isolated mesodermal defect.

L. Michaelis

1870. Lipoid Pneumonia (Non-inhalation) in Carcinoma of the Lung Treated by Radiotherapy

S. J. DE NAVASQUEZ, J. R. TROUNCE, and A. B. WAYTE. *Lancet [Lancet]* 1, 1206-1208, June 2, 1951. 7 figs., 9 refs.

A woman of 56 with bronchial carcinoma, for which she had been given x-ray therapy for 1 month, improved and 10 weeks later the radiograph was normal. Shortly afterwards, however, she had dyspnoea and pain and died within 24 hours of readmission. During the last stages x-ray examination showed a horizontal shadow which extended on both sides from the hilum to the pleura: this shadow corresponded with the fields exposed to x rays. At necropsy the growth was no longer in evidence. The burnt lung showed consolidation with foamy histiocytes containing cholesterol (non-inhalation lipoid pneumonia). It is suggested that the lipoid came from the breakdown of tumour tissue or from injured lung. Lipoid pneumonia was subsequently found in 4 consecutive cases of bronchial carcinoma in which x-ray therapy had not been given, and it was considered that x rays accelerated the process.

[Among pathologists lipoid pneumonia is (or should be) well known. It occurs most commonly in cases of retention bronchiectasis, in association with mild infection. If the obstructed bronchi are distended with clear mucus the related lung may show mucous consolidation, but not lipoid pneumonia. If, on the other hand, the distended bronchi contain mucus, some degree of lipoid pneumonia is almost constant. The condition is found with proximal but not with peripheral growths, unless the adjacent lung has been burnt. There is no mystery about the pathogenesis. Lipoid pneumonia is not due to the breakdown of tumour or lung tissue; nor is the condition atheromatous, as suggested more recently; it is simply inflammatory and results from the phagocytosis of effete inflammatory cells. In certain conditions macrophages ingest erythrocytes and accumulate haemosiderin. In other conditions, macrophages ingest inflammatory cells and gradually accumulate cholesterol. Between this condition and the condition which should be called inhalation oil pneumonia there are often marked morphological differences.]

D. M. Pryce

1871. Histopathology and Etiology of Pneumonia in Children Dying after Antibacterial Therapy

M. L. MENTEN and G. A. MCCLOSKEY. *American Journal of Pathology [Amer. J. Path.]* 27, 477-491, May-June, 1951. 10 figs., 15 refs.

Histological and bacteriological studies were made of the lungs of children who had died from pneumonia after treatment with penicillin, aureomycin, chloramphenicol, streptomycin, or dihydrostreptomycin. A mild type of

change restricted to the alveolar wall could be contrasted with a fulminating type with an exudation into the alveoli. No polymorphonuclear leucocytes were seen if no bacteria occurred. A virus was isolated from only 1 of 44 lungs, but the authors suggest a virus aetiology in most cases.

Brian E. Heard

1872. Atypical Pulmonary Inflammatory Reactions

E. F. GEEVER, K. T. NEUBUERGER, and E. K. RUTLEDGE. *Diseases of the Chest [Dis. Chest]* 19, 325-338, March, 1951. 8 figs., 29 refs.

In 10 patients dying from a variety of causes the following appearances were found in the lungs: fibrinoid degeneration of alveolar septa and blood vessels, proliferation of cells lining alveoli, hyaline membranes, fibrinous plugs in alveolar ducts, and occasional organization of these with the formation of Masson bodies. Others, such as Doniak, have regarded these changes as manifestations of chronic oedema due to left ventricular failure. The present authors, however, think that virus infection (the virus of atypical pneumonia) plays a part in their development and that conditions such as cardiac disease predispose to the infection.

[This cannot be denied, but there is no proof.]

D. M. Pryce

1873. The Early Changes of Pulmonary Tuberculosis in Lobectomy Specimens

E. NASSAU and W. PAGEL. *Tubercle [Tubercle, Lond.]* 32, 120-127, June, 1951. 8 figs., 4 refs.

The authors studied the gross and microscopical characters of tuberculous lesions in 32 lobectomy and 45 pneumonectomy specimens. The anatomical changes were extensive and ill-defined in 46 specimens, but were clear-cut in 26 lobectomy and 5 pneumonectomy specimens. The lesions took the form of large subpleural tuberculomata representing primary foci, primary cavities, or large post-primary foci with small, calcified, primary complexes elsewhere in the lungs.

The primary tuberculomata were large, round, lamellated lesions, for the most part solid, but showing early cavitation or microscopic evidence of liquefaction. The complementary foci in the regional lymph nodes were as a rule smaller and less conspicuous than the lung lesions, a reversal of the size relation of the two components of the primary complex in childhood. Primary cavities were found in 11 specimens. Most were solitary and associated with caseous or calcified bronchopulmonary lymph nodes. The average known duration of the disease in this group of cases was 2.6 years. Round post-primary foci were found in 1 pneumonectomy specimen and 7 lobectomy specimens. Inactive calcified primary complexes were identified in radiographs of the chest or were present in the specimens. The lesions were similar to the primary tuberculomata and showed signs of local recrudescence, including lamellation and an admixture of quiescent and progressive elements. The regional lymph nodes in these cases were non-caseous and the lung lesions were considered to be endogenous in origin and not the result of reinfection.

G. B. Forbes

1874. **Changes in the Liver in Congenital Syphilis.** (Über die Leberveränderungen bei der Lues connata) H. FLEGEL. *Zentralblatt für Allgemeine Pathologie und Pathologische Anatomie* [Zbl. allg. Path. path. Anat.] 87, 302-314, June 5, 1951. 32 refs.

The necropsy findings in 22 children with congenital syphilis, examined at the Pathological Institute of Jena University, form the basis of a study of the morbid anatomy and histology of the liver in this condition.

In a stillborn infant treponemata were numerous, but histological changes were not observed. In 4 cases treponemata were numerous and changes in the liver were mainly those of focal inflammation, which the author calls interstitial hepatitis or early cirrhosis. Areas of necrosis and granulation tissue were not infrequently seen in this group. In a group of 11 cases treponemata were absent, probably owing to efficient antisyphilitic treatment. Periportal round-celled infiltration and occasional foci of chronic inflammation were the main features in this group, but sometimes the smaller vessels were surrounded or even infiltrated by chronic granulation tissue and inflammatory cells, and sometimes the lobules of the liver contained such foci. In 6 cases treponemata were not found and changes in the liver were absent. It is pointed out that these findings do not agree with the descriptions in the classical text-books, and gummata were not seen. This series did not show the typical cirrhosis with biliary stasis usually described in earlier accounts.

E. Neumark

1875. **Tuberculosis of the Liver: Including a Report of Five Cases**

D. G. NEILL. *Medical Journal of Australia* [Med. J. Aust.] 1, 893-902, June 23, 1951. 18 figs., 24 refs.

The author reports 5 examples of tuberculosis affecting the liver, and draws attention to its rarity except in the miliary or disseminated form. Large tuberculomata often calcify and may be associated with extensive fibrosis. Tubercle bacilli may be found rarely or not at all, and the histological diagnosis from gumma is difficult.

[It is clear that up to the present the presence of tuberculous masses in the liver is simply an unusual necropsy finding, but in future needle biopsy (not mentioned by the author) may yield some surprises.]

J. W. McNee

1876. **Value of Gastric Biopsy in the Study of Chronic Gastritis and Pernicious Anaemia**

I. J. WOOD. *British Medical Journal* [Brit. med. J.] 2, 823-825, Oct. 6, 1951. 6 refs.

1877. **A Cytologic Study of Benign and Malignant Lesions of the Human Prostate, Urinary Bladder and Kidney**

A. E. BOTHE, A. J. DALTON, and F. O. ZILLESSEN. *Journal of Urology* [J. Urol.] 65, 1108-1117, June, 1951. 5 figs., 14 refs.

The authors studied the mitochondria and Golgi apparatus in surgical biopsies. They compared benign hypertrophy with carcinoma of the prostate, normal bladder with carcinoma of the bladder, and normal

kidney with carcinoma of the kidney. They found that there were differences between the benign and malignant cases in respect of the two elements studied. These methods are not yet applicable for routine diagnosis.

C. V. Harrison

1878. **Bone Marrow Embolism**

H. RAPPAPORT, M. RAUM, and J. B. HORRELL. *American Journal of Pathology* [Amer. J. Path.] 27, 407-433, May-June, 1951. 19 figs., 32 refs.

The authors found 13 cases of bone-marrow embolism of the lungs reported in the literature, 8 in some detail; the condition had been noted in rabbits after various experiments. They now report 27 more cases. Some of the emboli contained bone; death followed trauma, electrocution, or convulsions. The authors could not establish definitely whether an actual fracture was always necessary for its production, bone concussion being a possible cause. Some cases showed fat embolism as well; marrow embolism may have been a primary or contributory cause of death in these cases. As bone-marrow emboli were found in the lungs in 12 out of 200 cases of accidental death with fractures, their occurrence is more frequent than is generally realized.

Brian E. Heard

1879. **The Plasma Cells in Human Bone Marrow in Health and Disease.** (Le plasmacellule nel midollo osseo dell'uomo nella norma e nella patologia)

C. SACCHETTI. *Haematologica* [Haematologica] 35, 13-53, 1951. 11 figs., 29 refs.

Plasma cells in the bone marrow of 5 healthy people and of groups of 5 patients with carcinoma of the stomach, *Streptococcus viridans* infection, acute diphtheria, post-diphtheritic debility, cirrhosis of the liver, and nephrosis following nephritis were examined, and their relative numbers and the size of cells and nuclei determined. Normally there are 0.96 to 2.66% plasma cells in the bone marrow, but in cirrhosis they are increased to 3.74%. The average cell size is 14.4 μ and the average size of the nucleus is 8.5 μ . In cirrhosis the average cell size was 16.16 μ and average nuclear dimension 8.6 μ . With recovery from diphtheria the slightly enlarged cells become somewhat smaller.

E. Neumark

1880. **Electron Microscope Studies of Collagen from Normal and Diseased Tissues**

J. C. GALE. *American Journal of Pathology* [Amer. J. Path.] 27, 455-475, May-June, 1951. 12 figs., 12 refs.

After giving an account of some previous findings in this field, the author describes various samples of collagen. Using the metal-shadowing technique, he sought variations in structure and periodicity of the collagen fibres in normal and diseased tissues from human beings and from rabbits. The fibrils were freed of much of the amorphous ground substance by soaking in 2% sodium bicarbonate for about 30 hours. The significance of the variations found could not be estimated. The largest fibrils from any tissue were from a fibrosarcoma and measured up to 2,300 Å wide. Most diseased tissues showed no change.

Brian E. Heard

1881. Generalized Hypertrophic Osteoarthropathy. A Pathologic Study of Seven Cases

E. A. GALL, G. A. BENNETT, and W. BAUER. *American Journal of Pathology* [Amer. J. Path.] 27, 349-381, May-June, 1951. 22 figs., 32 refs.

Skeletal changes were examined in 7 patients with generalized hypertrophic osteoarthropathy, 6 having severe pulmonary disease and the seventh congenital heart disease. Subperiosteal new bone formation occurred in the long bones, beginning in the distal third of the bones of the forearm and leg. Joints showed chronic inflammatory changes in the synovia associated with degenerative changes in the articular cartilage. Clubbing of the digits was caused by soft-tissue changes, the predominant features being hyperaemia, oedema, increased amounts of loose-textured connective tissue, and mild chronic inflammation.

Theories of the aetiology of the condition are discussed, but no new views are advanced. R. H. Heptinstall

CLINICAL PATHOLOGY

1882. A Study of the Exfoliative Cytology in Patients with Carcinoma of the Oral Mucosa

P. W. MONTGOMERY and E. VON HAMM. *Journal of Dental Research* [J. dent. Res.] 30, 308-313, June, 1951. 4 refs.

Cytological smears were made from 15 cases of carcinoma of the oral mucosa and stained by Papanicolaou's method. A definite diagnosis was made in 13 cases, but it was doubtful in the other 2. Smears taken from the centre of the lesions were more reliable than those taken from the edges.

Smears were also prepared from the non-affected areas of oral mucosa in the above 15 cases and compared with smears from normal people. No significant differences were found. R. H. Heptinstall

1883. The Interrelationship of Blood and Urine Diastase during Transient Acute Pancreatitis

A. DANKNER and C. J. HEIFETZ. *Gastroenterology* [Gastroenterology] 18, 207-217, June, 1951. 5 figs., 23 refs.

The quantities of diastase and creatinine present in blood and excreted in the urine were measured at intervals of 1 to 2 hours during 13 attacks of transient acute pancreatitis occurring in 12 patients. The urinary excretion of diastase paralleled the blood diastase values throughout the attack. During a period of normal renal function high initial blood diastase values were followed in less than 2 hours by increased urinary excretion of diastase. Examination of the figures for creatinine concentration showed that acute pancreatitis, even in the absence of clinical shock, frequently impaired renal function, the effect being greatest 24 to 48 hours after the start of the attack and lasting for from 12 to 36 hours. When renal impairment occurred the blood diastase values returned to normal more slowly. If the renal damage occurred early the initial increase in urinary diastase values was delayed. J. E. Page

1884. Plasma Uric Acid in Aged and Young Persons

E. PRAETORIUS. *Journal of Gerontology* [J. Gerontol.] 6, 135-137, April, 1951. 2 refs.

1885. Neoplastic Cells in Bone Marrow Aspiration. [In English]

M. A. RUBINSTEIN and A. SMELIN. *Acta Haematologica* [Acta haemat., Basel] 5, 292-302, May, 1951. 4 figs., 20 refs.

The recognition of cells from metastases of malignant neoplasms in bone-marrow smears is not always easy, but in a series of 100 cases of advanced malignant disease 45 showed "malignant cells", mostly in clumps, in smears of sternal or iliac bone marrow. In 21 of 35 cases of mammary carcinoma, 3 of 14 cases of gastrointestinal carcinoma, 4 of 10 cases of lung cancer, and [surprisingly] in 11 of 21 cases of carcinoma of the genito-urinary tract (which included the prostate, ovaries, and ureter) neoplastic cells were found. Another feature of this investigation was the hypoplasia or aplasia observed in the bone marrow in about 75% of cases. When the marrow showed normal or increased cellularity neoplastic cells were not found so frequently as in aplasia. Anaemia and abnormalities in the peripheral blood were seen in only 10% of cases with neoplastic cells in the marrow. Sometimes bone-marrow biopsy showed neoplastic cells even though there was no radiological evidence of metastases. E. Neumark

1886. Diagnostic Value of the Glucose Content of Serous Pleural Effusions

W. L. CALNAN, B. J. O. WINFIELD, M. F. CROWLEY, and A. BLOOM. *British Medical Journal* [Brit. med. J.] 1, 1239-1240, June 2, 1951. 4 refs.

The authors, at the Whittington Hospital, London, have studied the value of glucose estimation in pleural effusions as a rapid means of determining whether these effusions are tuberculous. Sixty-one cases were examined, of which 25 were known to be tuberculous; 13 were due to congestive heart failure, 7 to carcinoma, 1 to leukaemia, 2 to pulmonary infarction, 1 was associated with pancreatitis, and 6 were post-pneumonic. A further 6 were undiagnosed. Fluoride was used to prevent glycolysis and the glucose was estimated by the Hagedorn-Jensen method. The specimens were obtained 2 hours after the last meal. In 24 cases the blood sugar level was within the normal range. All 30 non-tuberculous pleural effusions had a glucose level of over 60 mg. per 100 ml. of exudate, and in 24 of these the level was over 100 mg. per 100 ml. Of the 25 tuberculous cases, in 13 the glucose value was below 60 mg. per 100 ml. and in one in which it was high the patient had diabetes. The value in all 6 undiagnosed cases fell between 60 and 100 mg. per 100 ml. Four of these 6 were considered clinically and radiologically to be tuberculous, but bacteriological confirmation was lacking. In summary, a glucose level of less than 60 mg. per 100 ml. was found only in tuberculous effusions, whereas most non-tuberculous effusions had levels above 100 mg. per 100 ml. J. Maclean Smith

1887. Estimation of Renal Filtration by Thiosulphate and Maximum Tubular Reabsorption of Glucose.

(Определение фильтрации почек с помощью тиосульфата и максимальной реабсорбции глюкозы в канальцах)

G. F. BLAGMAN, E. I. ESTRIN, E. B. DVORKINA, and O. Y. MINZ. *Клиническая Медицина [Klin. Med., Mosk.]* 29, 59-67, May, 1951. 11 refs.

The formula for the clearance of any substance from the blood may be taken as $C = \frac{U \times V}{B}$, where U=urinary

concentration of the substance, B=the blood concentration, and V=the minute volume of urine. It follows that, for a substance filtered by the glomeruli and neither excreted nor reabsorbed by the tubules, the coefficient of clearance, C, equals the quantity of filtrate, F. Weberg suggested creatinine as fulfilling these conditions, and, by applying the above formula, estimated the renal filtrate in normal persons at 100 to 150 ml. per minute.

Inulin is not excreted by fish, which have no glomeruli but only tubules. It is excreted from the glomerular circulation of frogs but not from that of the tubules. The clearance coefficient of creatinine to that of inulin is as 1:12 : 1:39, so that creatinine cannot be regarded as being partly excreted by the tubules unless inulin is partly reabsorbed. Which explanation of the discrepancy is correct remains undetermined. The authors have employed sodium thiosulphate, which gives a clearance identical with that of inulin.

But filtration is not the only problem; there is also the reabsorption from the tubules to be taken into consideration in assessing renal function. Shenshon has demonstrated that the maximum reabsorption of glucose occurs when the blood glucose level reaches 500 mg. per 100 ml. This maximum reabsorption may be obtained from the formula $RMg = (B \times F) - (U \times V)$, where RMg is the maximum reabsorption of glucose, B and U the blood and urine concentrations of glucose, F the total urinary filtrate calculated from the clearance coefficient of thiosulphate, and V the minute volume of urine.

The procedure was as follows. After a control specimen of venous blood had been taken, 100 ml. of a 10% solution of sodium thiosulphate in 2% sodium bicarbonate was injected within 10 minutes. The bladder was evacuated; after 15 minutes blood was again taken from a vein: 15 minutes later the urine was collected: 15 minutes later a second blood specimen was taken; and after another 15 minutes a second specimen of urine. From these data the thiosulphate clearance, and hence the total filtration volume, was obtained.

For estimating the maximum reabsorption of glucose, 15 ml. of 22% thiosulphate in 2% sodium bicarbonate with 90 ml. of 40% glucose was injected intravenously in 5 minutes, after a preliminary blood specimen had been taken. The bladder was first evacuated and then an intravenous drip consisting of 35 ml. of 22% thiosulphate in bicarbonate and 480 ml. of 40% glucose was given at the rate of 5 ml. per minute. Blood and urine were collected at the end of 40 minutes, and their thiosulphate content estimated by the iodine method, the urinary

glucose level polarimetrically, and the blood glucose level by Hagedorn's method. From these data the filtration rate and maximum reabsorption were calculated.

In 11 patients with no apparent renal dysfunction the filtration varied from 101 to 164 ml. per minute, and the maximum reabsorption from 189 to 421 mg. per minute. In 3 cases of acute nephritis the filtration rate varied between 60 and 132 ml. per minute, and the maximum reabsorption between 96 and 360 mg. per minute.

In 3 cases of chronic nephritis without uraemic symptoms the figures were 87 to 185 ml. and 218 to 470 mg. respectively; but in 3 cases of azotaemia (1 with pyonephrosis) the filtration rate was 6 to 41 ml. and the reabsorption 6 to 149 mg. per minute. In 4 cases of lipid nephrosis filtration rate was 84 to 234 ml. and reabsorption 361 to 660 mg. per minute; in other words, both figures tended to be higher than normal. Large doses of ketosteroids such as testosterone, deoxycortone acetate, and oestrogens produced no significant change, except that in a case of Addison's disease the figures, previously low, rose to normal.

Whereas inulin causes unpleasant side-effects (rigors, pyrexia, and pain in the loins), the routine described above appears to have been well tolerated by most of the patients and is regarded as a safe method of estimation of these factors in renal function. *L. Firman-Edwards*

1888. The Excretion of Pantothenic Acid in the Urine in Young and Old Individuals

V. SCHMIDT. *Journal of Gerontology [J. Gerontol.]* 6, 132-134, April, 1951. 6 refs.

1889. A Study of Hepatic Function in Man before and after Partial Resection of Liver

F. V. FLYNN and J. M. WALSH. *British Medical Journal [Brit. med. J.]* 1, 1484-1486, June 30, 1951. 2 figs., 18 refs.

Biochemical studies in man after partial hepatectomy showed few significant changes in a number of tests performed 5 days, and between 50 and 100 days, after operation. Few, if any, previous investigations of this nature are available in the literature. In the cases described approximately 16% of the liver was removed for primary liver-cell carcinoma, and there was no histological evidence of cirrhotic change.

Regeneration of the remainder of the liver appeared to take place rapidly. No change was observed after operation in the values revealed by the following tests: plasma prothrombin, serum bilirubin, and blood urea concentration, hippuric acid synthesis, bromsulphalein clearance, and serum alkaline-phosphatase level. An increase in urinary urobilinogen followed the liver resection, but was also noted in several control patients who had undergone comparable operations, but not involving the liver. The thymol turbidity and serum flocculation tests gave positive results after the partial hepatectomy and remained abnormal for some months, possibly due to liver-cell damage at the site of the resection rather than to actual loss of liver tissue. No specific changes occurred post-operatively in amino-acid metabolism. *Thomas Hunt*

Microbiology

1890. The Life Cycle of *Actinomyces bovis*

E. O. MORRIS. *Journal of Hygiene [J. Hyg., Camb.]* 49, 46-51, March, 1951. 2 figs., 24 refs.

A study was undertaken of 10 bovine and 2 human strains of *Actinomyces bovis*, all capable of growing anaerobically or in 10% carbon dioxide, but none under completely aerobic conditions. Two types of colony formation were noted, adherent and non-adherent; continued subculture on the same medium often led to the former changing to the latter. The adherent colonies consisted of filaments composed of a number of individual cells, while in the non-adherent colonies the individual cells were usually separate.

The author demonstrates that *Actinomyces bovis* passes through a complete life cycle, the spore germinating to produce a haploid generation from which a diploid generation arises by conjugation of 2 specialized haploid cells.

R. B. Lucas

VIRUSES

1891. Lethal Infection with Coxsackie Virus of Adult Mice given Cortisone

E. D. KILBOURNE and F. L. HORSFALL. *Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol., N.Y.]* 77, 135-138, May, 1951. 3 refs.

The fact that the adult mouse has proved to be insensitive to Coxsackie virus infection led the authors to investigate whether previous injection of cortisone would affect this insusceptibility. Experiments were carried out on Rockefeller Institute Swiss mice—both "suckling" mice (less than 1 day old) and "adult" mice which were sexually mature, of an average weight of 6 g., and 3 to 4 weeks old. Two strains of Coxsackie virus—Conn. No. 5 and RB—were used. Antisera for the neutralization test were heated at 56° C. for 30 minutes. Cortisone acetate was injected subcutaneously in 2.5- to 5-mg. doses; most of the adult mice survived this dose for at least 8 days, when the experiment was terminated. Pfanstiehl peptone broth and 0.85% NaCl buffered to pH 7.2 with phosphate were used for control injections.

One subcutaneous injection of cortisone was given to mice 1 to 2 hours before inoculation of the virus. Light ether anaesthesia was induced when mice were injected by the intracerebral route. Control groups of mice were given injections of both cortisone and broth in quantities and by routes identical with those employed in virus-inoculated animals. When the intraperitoneal route was used the viral suspensions were administered in amounts approximately proportional to the size of the mice inoculated (0.05 ml. virus suspension to 1.5 g. of mouse). All viral inocula contained penicillin and streptomycin and were bacteriologically sterile.

Three days after inoculation all mice given cortisone and virus were dead, while controls given either virus or cortisone were alive after 8 days. It was ascertained that in cortisone-injected mice viral multiplication took place, the lethal effect was serially transmissible, and multiplication of virus and lethal effect could be neutralized by specific antiserum. It was found also that 17-week-old mice weighing 35 g. are sensitive to the lethal infection if they have previously been given an injection of 7.5 mg. of cortisone. The infection of the adult mice pretreated with cortisone took place also with Coxsackie virus which had not previously been passed through infant mice, but which was derived directly from a human source (stool).

Intraperitoneal injection proved fatal in 3 days, while mice receiving virus by the intracerebral route succumbed more slowly, dying 7 days after inoculation. It should be pointed out, however, that the intracerebral inoculation was only one-tenth the volume of that given intraperitoneally. A 1-in-100 dilution of brain tissue from mice which had received an intraperitoneal injection of infected stool promptly killed all animals when passed with normal mouse serum, but caused no evident disease or death in the presence of specific immune serum against the RB strain of virus.

Negative results were obtained from control mice in all experiments.

Observations on the adult mice pretreated with cortisone and infected with Coxsackie virus revealed that 2 to 3 days following inoculation some animals became temporarily hyperexcitable and showed huddling, ruffled fur, arched backs, and laboured respiration with progressive unresponsiveness and lethargy proceeding to stupor and sudden death. Paralysis, tremor, and convulsions were not, however, noticed.

J. W. Czekalowski

1892. Endocrines and their Relation to Influenza Virus Infection

S. S. KALTER, H. J. SMOLIN, J. M. McELHANEY, and J. TEPPERMAN. *Journal of Experimental Medicine [J. exp. Med.]* 93, 529-538, June 1, 1951. 4 figs., 18 refs.

The authors describe the effect of testosterone, ACTH, and cortisone on proliferation of influenza virus in mice. In all experiments a "challenge" dose of approximately 500 or 1,000 LD₅₀ was given to each mouse; over the following 48 hours groups of at least 5 were killed, their lungs weighed and then broken up in a Waring blender, and the virus content titrated. For the testosterone experiments 200 male mice about 6 weeks old were either castrated or sham-operated (laparotomy without orchidectomy) and grouped as follows: (a) untreated castrates; (b) testosterone-treated castrates; (c) untreated sham-operated controls; and (d) testosterone-treated sham-operated controls. After three weekly injections of

testosterone or Wesson oil (controls) the challenge dose of virus was given. In 24 hours normal animals receiving testosterone contained most virus, and untreated castrates least; after 48 hours this difference was present but less marked. A similar experiment was performed on groups of 5- to 6-week-old mice (without previous operation) following 7- to 12-day courses of ACTH or cortisone. After the challenge dose of virus, mice treated with ACTH or cortisone contained less virus than controls. During the various experiments with testosterone, ACTH, and cortisone the time of death and the extent of lung consolidation following virus inoculation were compared between small groups of mice without any significant differences being found.

In a cautious discussion the authors point out that whereas testosterone increases protein anabolism and virus proliferation, ACTH and cortisone increase protein catabolism but decrease virus proliferation. This suggests a correlation between alterations in protein metabolism and virus proliferation under the conditions of the experiments.

Peter Story

BACTERIA

1893. Penicillin-resistant Staphylococcal Infection in a Maternity Hospital

M. BARBER, F. G. J. HAYHOE, and J. E. M. WHITEHEAD. *Lancet* [Lancet] 2, 1120-1125, Dec. 17, 1949.

A study was made of the incidence of penicillin-resistant strains of staphylococci in a maternity hospital in which about one-seventh of the infants suffered from infections with this organism. Of 42 such infants, 36 yielded penicillin-resistant strains only, and a further 3 mixed cultures with both resistant and sensitive strains. About two-thirds of the medical and nursing staffs were found to be nasal carriers, and of the strains recovered from these carriers about three-quarters were penicillin resistant. The majority of the typable resistant organisms belonged to the same phage type, 52A. The nasal-carrier rate in a small number of the domestic staff in this hospital was about the same as that of the medical and nursing staff, but resistant strains were much less common. A comparative study of 62 women in a large London shop showed that about half were nasal carriers of staphylococci, but none of the strains recovered was penicillin resistant.

Of the 44 strains of staphylococci recovered from infected lesions, all had a sensitivity to streptomycin and 42 had a sensitivity to sulphathiazole that was equal to that of the Oxford staphylococcus; 2 strains had greater resistance to sulphathiazole.

G. Payling Wright

1894. Some Observations on Survival of Pathogenic Bacteria on Cotton-wool Swabs. Development of a New Type of Swab

S. D. RUBBO and M. BENJAMIN. *British Medical Journal* [Brit. med. J.] 1, 983-987, May 5, 1951. 1 fig., 20 refs.

Different species of bacteria survive for greatly varying periods of time on cotton-wool swabs as sent to laboratories for examination. The amount of

moisture in the swab and the batch of cotton-wool used influence the survival times, but not uniformly for all bacterial species. A new type of swab was devised and found valuable for routine use, as it favoured the survival of bacteria, with the possible exception of *Neisseria*. Wool was rolled on wooden applicators and dipped in ox serum. After drying in an incubator the swabs were sterilized in the autoclave. This treatment made the cotton-wool adhere firmly to the swab stick.

Scott Thomson

1895. Effect of Cortisone on Pneumococcal Bacteraemia

R. G. WHITE and A. H. E. MARSHALL. *Lancet* [Lancet] 1, 891-892, April 21, 1951. 4 figs., 7 refs.

The authors report their investigation of the effect of cortisone on pneumococcal bacteraemia. Into the ear vein of each of 8 rabbits 1 ml. of a broth culture of pneumococci was injected. The animals were paired, and one of each pair received cortisone while the other served as an untreated control. The treated animals were given cortisone in a dose of 15 to 20 mg. 20 hours and 1 hour before the injection of the culture, and 24 and 48 hours after the injection (if the animal was still alive). At varying intervals 1 ml. of blood was withdrawn from the vein of the opposite ear and the number of organisms in the sample estimated by the pour-plate technique.

In the control animals the number of organisms diminished rapidly; in the cortisone-treated group there was a slight initial fall, but thereafter a rapid increase, in the bacterial content of successive samples. The results of one experiment are given below.

Time after Injection	Organisms per ml. (thousands)	
	Control	Treated
Immediately ..	5,600.0	4,900
10 minutes ..	800.0	774
1 hour 20 minutes ..	20.7	120
3 hours ..	9.3	414
5 " ..	2.5	1,400
24 " ..	1.2	13,000

G. B. Forbes

1896. Streptomycin-dependent Tubercle Bacilli

E. A. DOANE and E. BOGEN. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 64, 192-196, Aug., 1951. 1 fig., 10 refs.

1897. Outbreak of *Aerobacter* Infections on Infants' Wards

M. H. D. SMITH, C. G. LOOSLI, and M. H. RITTER. *Pediatrics* [Pediatrics] 7, 550-562, April, 1951. 1 fig., 38 refs.

During an investigation into the control of air-borne infection by means of triethylene glycol vapour there occurred an outbreak of infection due to an encapsulated Gram-negative bacillus not hitherto described. In the course of the investigation two infants' wards

were used, one being kept as a control while in the test ward triethylene glycol was vaporized. Two nasopharyngeal cultures were taken from each infant on admission, two each week thereafter, and one at the time of discharge. Nose and throat cultures were also taken from members of the staff. It was planned to study the introduction and spread of various types of pneumococci and haemolytic streptococci, but soon after the investigation was started there began to appear in the nasopharyngeal cultures of patients an encapsulated Gram-negative rod. This organism, designated as *Aerobacter carter*, was found to be a member of the *Aerobacter-Klebsiella* group, and showed capsular swelling with Types 23 and 32 pneumococcal antisera. Triethylene glycol vapour exerted no influence on the incidence of infection with this organism: in the test ward 25 out of a total of 183 patients harboured the organism, whereas in the control ward 25 out of 178 patients became infected.

With regard to mode of infection, direct patient-to-patient transmission seemed to be entirely excluded, as there were separate cubicles for each patient. Indirect contact by hands or fomites could be considered rare, as a careful technique was used. Healthy adult carriers as a source of infection seemed unlikely. The air and dust in the ward were, however, found to be heavily contaminated, and remained so for a period of 2 months; also at least 2 patients who harboured the organism in the nasopharynx had a purulent nasal discharge. Thus it appeared that dispersion occurred mainly from respiratory discharges—a view supported by the fact that the outbreak was self-limiting, ceasing abruptly with the onset of warm weather and the disappearance of respiratory disease.

R. B. Lucas

1898. Laboratory Diagnosis of Urinary-tract Infection with Special Reference to Lactose-fermenting Coliform Strains

J. B. ENTICKNAP and B. J. STEPHENS. *British Medical Journal* [Brit. med. J.] 1, 1119–1123, May 19, 1951. 1 fig., 9 refs.

An investigation was made of 114 strains of coliform organism isolated from 86 patients with urinary-tract infections, together with 51 strains isolated from the urine as contaminants. The Ministry of Health classification for coliform organisms in water proved unsuitable for classifying these strains, there being 22 strains (12.1%) which could not be classified. A simple classification based on the production of gas at 44° C. and the formation of mucoid colonies is suggested. These properties could be noted in 24 hours. The centrifuged deposit of urine itself could be used as the inoculum for noting production of gas.

From infected urines the strains were *Bacterium coli*, 46%; atypical coliform bacteria, 46%; *Aerobacter aerogenes*, 8%. Atypical strains were more common as contaminants. *Aero. aerogenes* strains and half the atypical coliforms were slightly resistant to sulphonamides. *Bact. coli* strains were more sensitive; sensitivity to sulphonamide and sensitivity to penicillin tended to run parallel. *Bact. coli* infections occurred significantly

less frequently in patients with organic obstruction of the urinary tract than in patients with pyelitis.

D. G. ff. Edward

1899. Isolation of Salmonellae from Faeces of Domestic Animals

H. W. SMITH and A. BUXTON. *British Medical Journal* [Brit. med. J.] 1, 1478–1483, June 30, 1951. 16 refs.

Faeces from cattle, sheep, horses, pigs, goats, chickens, turkeys, ducks, and geese were examined for salmonellae. Specimens were inoculated into selenite F and into tetrathionate broth; subcultures from these were made on plates of desoxycholate-citrate medium containing 1% sucrose and 1% salicin; suspicious colonies were tested for indole and urease production, and colonies negative to these tests were streaked on desoxycholate-citrate medium containing 1% dulcitol but no lactose, sucrose, or salicin. Colonies which fermented dulcitol and/or agglutinated with polyvalent O serum were transferred to plain Craigie tubes (to induce motility) and then subcultured on moist agar slopes. Identification was made by serological and biochemical tests.

The findings were as follows: (1) Healthy adult animals. Of 650 turkeys, 2.5% were found to be excreting salmonellae (*Salmonella typhimurium*, 11; *Salm. anatum*, 4; *Salm. tennessee*, 1); of 100 geese, 2 were found to be excreting these organisms (*Salm. typhimurium*, 1; *Salm. thompson*, 1); of 500 ducks, 1.2% (*Salm. meleagridis*, 1; *Salm. typhimurium*, 5); of 600 pigs, 0.7% (*Salm. meleagridis*, 3; *Salm. typhimurium*, 1); of 750 chickens, 0.7% (*Salm. typhimurium*, 2; *Salm. pullorum*, 2; *Salm. anatum*, 1); of 750 cows, 0.4% (*Salm. dublin*, 3); of 500 horses, 0.2% (*Salm. thompson*, 1); and of 500 sheep, nil. (2) Animals suffering from diseases other than primary salmonella infection. Of 500 chickens, 1.6% were found to be excreting salmonellae (*Salm. typhimurium*, 4; *Salm. pullorum*, 2; *Salm. thompson*, 1; *Salm. senftenberg*, 1); of 500 cows, 0.6% (*Salm. dublin*, 3); of 500 horses, 0.4% (*Salm. dublin*, 1; *Salm. thompson*, 1); and of 130 sheep, 100 goats, and 33 pigs, nil. (3) No salmonellae were isolated from 430 cows, 420 chickens, 155 ducks, and 63 turkeys exhibited in national shows in Britain.

Selenite medium was found to be superior to tetrathionate broth as an enrichment medium, but a greater number of positive specimens were found by the use of both media. The authors discuss the significance of symptomless animal excretors of salmonellae from the public-health and agricultural aspects.

Joyce Wright

1900. The Pathogenicity of the Spores of *Clostridium botulinum*

J. KEPPIE. *Journal of Hygiene* [J. Hyg., Camb.] 49, 36–45, March, 1951. 6 figs., 12 refs.

Loeffler's solid serum having been found the most suitable medium for producing a high proportion of spores, batches were inoculated with a few drops of cooked-meat cultures of 2 type-A strains of *Clostridium botulinum* and incubated in anaerobic jars at 37° C. for 3 to 6 weeks. The contents of the tubes were

filtered through glass wool and the spores were washed with distilled water by repeated centrifugation. Liquor from the liquified Loeffler cultures contained 100,000 mouse LD50 per ml., but the toxicity of the supernatant from the first and second washings was only 1,000 LD50 per ml. The supernatant discarded after the third washing was toxic only when 0.1 ml. was injected, and after it had been exposed to heat at 80° C. for an hour the distilled water suspending the stock suspension was non-toxic in a volume of 0.5 ml.

White mice were given intramuscular injections in a volume of 0.1 ml. and died within 2 to 5 days thereafter with local and general symptoms of botulism. Microscopical examination of the local lesions in the muscle showed that the spores did not germinate. Mice treated prophylactically with type-A botulinum toxoid or with type-A antitoxin were completely immune to the spores, thus confirming that death resulted from the specific toxæmia.

In order to determine whether toxin existed within the spores, stock suspensions were incubated at 34° C. in various extracting fluids in which the toxin could survive, but which were unsuitable for the germination of spores. The fluids were then tested for toxin by the injection of 0.5 to 1.0 ml. into mice. In no instance did the mice die or show symptoms of botulism.

Spores were disintegrated in a Mickel shaking machine: positive results were now obtained. That the toxin was released from within the spores was proved by the fact that the supernatant of the stock spore suspension was innocuous in a volume of 0.5 ml., and the heat and antitoxin treatments individually could destroy a potent concentration of toxin had it been present on the outside of the spores or free in the suspending fluid.

When mice were injected intramuscularly with mixtures of spores and 2.5% calcium chloride solution, there was only slight transient swelling of the leg, but when toxin-free spores were included in the injection, lameness and local paralysis of the leg passed to fatal general botulism in 2 to 5 days. When calcium chloride was included in the intramuscular injection the LD50 was much smaller and contained far fewer spores than could cause a fatal toxæmia without germination occurring.

R. B. Lucas

SPIROCHAETES

1901. The Treatment of Experimental Leptospirosis in Animals. (Tierexperimentelle Untersuchungen über die Therapie der Leptospirosen)

P. UHLENHUTH and K. E. SCHOENHERR. *Zeitschrift für Immunitätsforschung [Z. ImmunForsch.]* **108**, 289-300, June 22, 1951. 2 refs.

The authors used golden hamsters for their work on the treatment of experimental leptospirosis. These animals, which were between 4 and 6 weeks old and weighed 40 g., were infected with a *Leptospira canicola* strain, the virulence of which had been raised by animal passage so that 0.5 ml. of a liver suspension proved lethal in an average time of 79 hours. The authors recorded the pathological changes and the spread of the leptospires

in the organs of hamsters killed 24, 40, 48, and 72 hours after infection. The authors then studied the effects on infected hamsters of the administration of different sera, aureomycin, terramycin, and chloramphenicol. Injections of 0.1 ml. serum were given 8-hourly for 3 days, starting at the time of infection or 16 or 40 hours later. Good results could be obtained only with abnormally high doses of a rabbit immune serum made with a homologous strain of *L. canicola*. The results of treatment with antiserum derived from two sources were bad, and leptospires could be demonstrated in the kidneys of all hamsters whose death was delayed.

The sensitivity of several leptospires to aureomycin was tested, 1 mg. being given intraperitoneally every 8 hours for 3 days. This therapy was started at the time of the infection or from 8 to 64 hours after infection. If the therapy was started 40 hours after infection, 50% of the hamsters could be saved; if 48 hours after, 27%; if 56 hours after, 1 in 14 survived. Those hamsters which survived were perfectly normal; pathological lesions had healed and no chronic leptospirosis resulted. The results with terramycin (0.17 mg.) were better, 67%, 20%, and 25% respectively being saved if treatment was started 48, 56, and 64 hours after infection. Chloramphenicol proved to be without effect. It is pointed out that a natural infection is not necessarily comparable to an artificially induced one.

A review is given of a number of publications on the use of aureomycin and streptomycin in leptospirosis in man and dogs.

Margaretha Adams

1902. The Effect of Chemotherapeutic Agents and Antibiotics on Pathogenic Leptospires. (Die Wirkung von Chemotherapeutika und Antibiotika auf pathogene Leptospiren)

H. W. SCHLIPKÖTER and M. BECKERS. *Zeitschrift für Immunitätsforschung [Z. ImmunForsch.]* **108**, 301-317, June 22, 1951. 2 figs., bibliography.

After a review of the history of the treatment of leptospirosis, the authors describe the results of a series of tests to determine the bacteriostatic action in Korthof's medium of several chemotherapeutic and antibiotic agents on 6 pathogenic strains of *Leptospira*.

Mepacrine had a marked bactericidal action, but in a concentration higher than can be reached in the body. Penicillin had a bacteriostatic action at a concentration of less than 0.14 unit per ml. Streptomycin was less effective than penicillin, aureomycin more effective than chloramphenicol for all strains except for *Leptospira autumnalis*. Terramycin had the greatest bacteriostatic action. Only with aureomycin and terramycin can blood concentrations be reached in man higher than the minimum bacteriostatic concentrations *in vitro*.

The literature on the use of these agents in clinical leptospirosis is discussed. One experiment *in vivo* is described with 16 golden hamsters infected with *Leptospira icterohaemorrhagiae* and treated orally with different concentrations of terramycin at different intervals after the infection. Only high doses (3,000 µg., equivalent to 1.5 to 2 g. for man) could save the

hamsters from leptospiral infection if given either at the time of infection or 24 hours after infection. A dose of 5,000 to 12,000 μ g. per day made recovery possible even after clinical symptoms had developed. Nothing is yet known about the absorption of orally administered terramycin. Results of experiments *in vivo* with terramycin, aureomycin, and mepacrine will be published shortly.

Margaretha Adams

1903. A New Method of Demonstrating Vincent's Spirochaetes. (Mise en évidence du spirochète de Vincent sur une nouvelle base)

S. C. VAGO. *Schweizerische Zeitschrift für Allgemeine Pathologie und Bakteriologie* [Schweiz. Z. allg. Path.] 14, 34-41, 1951. 25 refs.

While searching for a method of staining Vincent's spirochaetes that would be better than thionine or the Gram method the author examined, without success, the possibilities of 126 chemical substances used in bacteriological technique and also many other substances. The only one that was useful was a concentrated solution of the disodium salt of dibromohydroxymercurifluorescein, known as "mercurochrome" and by other names. This coloured the spirochaetes pale yellowish-red, but the colour needed intensification and bacteria took the same colour. Modification of the temperature, pH, and duration of the staining gave no better result, and combination of mercurochrome with other stains showed that most stains were precipitated and that the yellowish-red given by mercurochrome was turned greyish or that the colour was altered without being intensified. The one substance that intensified the stain was Merck's methyl violet ("pyoktanin"). Used after mercurochrome this stained the spirochaetes a dark bluish-black, and their contours were clear.

The author's method is now as follows: Spread the material thinly on a slide and dry in the air. Neither heat nor fixation is necessary. Stain with a saturated aqueous solution of the disodium salt of dibromohydroxymercurifluorescein for 5 minutes. After the mercurochrome, stain for 5 minutes with a saturated aqueous solution of pyoktanin (Merck's methyl violet). Wash in water and dry. Both stain solutions keep indefinitely and can be made with either ordinary or distilled water. At least 3 minutes in the stains should be given, but after that time the exact duration does not matter. Differentiation is not possible and the pH of the solutions used makes no difference, so that the method is simpler than the methods of Gram and Giemsa.

The spirochaetes are stained an intense bluish-black on an unstained background, but the fusiform bacilli often present with them, and also cells and other microorganisms, take the stain with the same intensity. Details in the organisms are not made visible, but the outlines of the spirochaetes are well preserved. The spirochaetes appear about one-fourth as big again as those stained by silver-impregnation methods, about half as big again as those stained by the methods of Griesbach or Tunnickliff, and almost twice as big as those stained by the methods of Gram or Giemsa.

G. Lapage

IMMUNITY

1904. A Study of the Hemagglutinin Produced in Response to the Administration of P³² Tagged Erythrocytes

S. G. COHEN. *Annals of Allergy* [Ann. Allergy] 9, 281-291, May-June, 1951. 4 figs., 26 refs.

Ten rats were injected with chicken erythrocytes and the same number with sheep erythrocytes. These blood cells had been labelled with ³²P. The haemagglutinin of the resultant antiserum was then isolated by means of non-labelled erythrocytes. The antigen-antibody complex thus produced did not contain radioactive elements. This shows that antigen is not incorporated into the antibody molecule during its synthesis.

H. Herxheimer

1905. Paralysis following Immunising Injections. Measures Calculated to Diminish the Risk

G. BOUSFIELD. *Lancet* [Lancet] 1, 1028-1032, May 12, 1951. 3 figs., 9 refs.

This paper was inspired by a remark made to the author to the effect that paralytic poliomyelitis following injections of diphtheria prophylactic or combined diphtheria toxoid and pertussis vaccine seemed to occur less often in infants under 1 year of age than in older children. Study of the Registrar-General's returns seemed to confirm this, and the author concludes that, as the disease in recognizable form is relatively infrequent under the age of 6 months, it ought to be possible to take advantage of this fact in any attempt to avoid paralytic sequelae to injections of diphtheria and possibly other prophylactics. If such treatment can be shown to be both effective and durable, it would seem that inoculation against diphtheria should be undertaken as early in life as possible.

The author quotes figures, including his own, proving that infants can be immunized successfully at the age of 2 to 5 months and that in most cases the immunity holds good some 18 months to 2 years later. As regards the route of injection, it is now fairly generally accepted that intramuscular injections made when poliomyelitis is prevalent tend occasionally to be followed by paralysis of that muscle or of an associated group. The diphtheria prophylactics which seem to be chiefly connected with such lesions after intramuscular inoculation are alum-precipitated toxoid (A.P.T.) combined with pertussis vaccine and, to a less extent, A.P.T. given alone. It is therefore necessary to find a prophylactic which can be given subcutaneously without the production of excessive local reaction. Three preparations have been investigated: (1) Holt's purified toxoid (P.T.A.P.), given as two subcutaneous injections of 0.3 ml. at a month's interval to children aged 1 year or less, has yielded a Schick conversion rate of 99.7% without the production of objectionable reactions. (2) Because it was feared that the aluminium hydroxide in prophylactics such as A.P.T. might be the irritant involved in the production of post-injection poliomyelitis paralysis, it was resolved to use an antigen without

mineral carrier. A highly purified toxoid in buffered saline solution has been investigated. It is given as three subcutaneous injections of 0.5 ml. and has produced a Schick conversion rate of 99.2% in children aged 1 year or less. (3) To make the immunization of the very young infant as efficient as possible, and to overcome the difficulty occasioned by the infant's having a fairly large amount of residual, maternally-bestowed antitoxin in its blood, an experimental prophylactic, F.P.T. (fluid and phosphate toxoid), has been prepared and preliminary work on it is in progress. The fluid toxoid is designed to fix the child's antitoxin by combining with it rapidly, leaving the adsorbed toxoid to exercise its more potent stimulus unhampered. In 154 small children a conversion rate of 98.7% has been obtained.

The author concludes by stating that the logical approach to the problem is to inoculate infants subcutaneously with suitable diphtheria prophylactics as early as possible in life, and certainly before the age of 6 months. Among prophylactics at present generally available which should prove suitable are fluid toxoid (purified toxoid in buffered saline solution) in 3 monthly injections of 0.5 ml., or 2 well-spaced injections of 0.3 ml. of P.T.A.P. In treating infants who have not previously been shown to be Schick-positive and who may still possess maternally bestowed antitoxin, an interval of 3 or 4 months between the two injections of P.T.A.P. is advised.

J. V. Armstrong

1906. Immunity to Tuberculosis Studied by means of Radioactive Bacilli. (Quelques expériences concernant l'immunité antituberculeuse, effectuées à l'aide de bacilles radio-actifs)

L. STRÖM and G. WIDSTRÖM. *Acta Paediatrica [Acta paediatr., Stockh.]* 40, 213-217, May, 1951. 5 refs.

B.C.G. bacilli grown in Dubos's liquid medium containing radioactive phosphorus were washed and injected intravenously into small groups of guinea-pigs, some of which had been infected at varying intervals previously with virulent *Mycobacterium tuberculosis* or had been vaccinated with B.C.G., while others which had had no previous contact with tubercle bacilli served as controls. Animals were killed 12 and 24 hours after injection and their tissues, blood, and urine assayed for radioactivity. The lymph nodes of the control animals after 24 hours showed the highest level of activity, but the concentration in the urine was higher in the vaccinated animals than in the controls.

J. E. M. Whitehead

1907. The Effect of ACTH and Cortisone on Certain Immunologic Mechanisms including Reversed Anaphylaxis

C. E. ARBESMAN, E. NETER, and L. F. BERTRAM. *Journal of Allergy [J. Allergy]* 22, 340-349, July, 1951. 13 refs.

Forssman antibodies were prepared and the least amount necessary to produce fatal shock by intracardial injection determined in normal guinea-pigs. This amount varied from 0.25 to 1 ml. ACTH was injected in doses of 0.1 to 20 mg. 8 to 24 hours before the intracardial injection of Forssman antibodies. Doses between 0.5 and 2 mg. seemed to give some protection, but this effect was absent with higher and lower doses.

Cortisone had no effect. In another series of experiments reversed anaphylaxis was produced by the injection of rabbit antiserum into guinea-pigs. Here 13 of the 20 untreated animals died in shock, whereas of the 20 treated with 6 and 10 mg. of ACTH, only 6 died. Under cortisone 1 animal out of 20 died, compared with 8 when untreated. In ordinary active and passive anaphylaxis no protective effect of ACTH or cortisone was found. These substances were also given early during the period of sensitization, and the absence of any effect shows that they do not prevent the formation of antibodies. In 3 ragweed-sensitive patients who were treated with about 100 mg. of ACTH for one week the reagin titre of the serum did not change.

H. Herxheimer

1908. Detection of Q-fever Antibodies by the Antiglobulin Sensitisation Test

R. R. A. COOMBS and M. G. P. STOKER. *Lancet [Lancet]* 2, 15-17, July 7, 1951. 9 refs.

The antiglobulin sensitization test has been adapted to detect antibodies in Q fever. Mixtures of a suspension of *Rickettsia burnetii* and serial dilutions of serum, after preliminary incubation, were centrifuged in the angle centrifuge. The deposit of organisms was washed three times and finally suspended in saline. The organisms were then tested for agglutination using an anti-human-globulin serum. *Rickettsiae* adsorbed antibody, when this was present in the serum, and so could be agglutinated by an antiserum to globulin.

A number of sera were examined by this method and also by the direct agglutination and haemolytic complement-fixation tests. Sixteen sera, including 8 from known cases of Q fever, which gave positive complement-fixation reactions, gave higher titres with the sensitization test. The latter test proved more reliable than the direct agglutination test. Only partial agglutination at a dilution not exceeding 1 in 10 was noted in 6 of 11 sera negative to the complement-fixation test, including 1 from a case of atypical pneumonia.

The antiglobulin sensitization test was thus shown to be more sensitive than the two other tests, but further investigation will be necessary before its specificity can be established.

D. G. ff. Edward

1909. Mouse-protective Potency Assay of Typhoid Vaccine, as Performed at the Army Medical Service Graduate School

H. C. BATSON, M. BROWN, and M. OBERSTEIN. *Public Health Reports [Publ. Hlth Rep., Wash.]* 66, 789-805, June 22, 1951. 24 refs.

The method used at the U.S. Army Medical Graduate School, Washington, D.C., for testing potency in typhoid vaccines is described. [The original paper, which contains full details, should be consulted by those engaged in vaccine production.] The method is an active-immunity mouse-protection test, in which the potency of the vaccine under test is compared with a standard reference vaccine. Mice receive 1 intraperitoneal inoculation and are challenged 6 days later by an intraperitoneal injection of living typhoid bacilli of a selected strain, suspended in 5% hog gastric mucin.

D. G. ff. Edward

Paediatrics

1910. Bacterial Flora and Bacterial Counts of Infants' Bottle Feeds

J. WRIGHT. *British Medical Journal* [Brit. med. J.] 2, 138-143, July 21, 1951. 1 fig., 21 refs.

An account is given of the bacterial flora found in 300 infants' bottle feeds sampled in London in 1946-8. Sample feeds were obtained from children's hospitals, an infectious diseases hospital, residential nurseries, and an infant welfare centre. The feeds were made up from cows' milk, dried milk, expressed human milk, and clear fluids such as saline. Only 19% of the feeds sampled proved sterile, the remainder containing up to 880,000,000 organisms per ml. Milk feeds were found to be infected most often with micrococci, aerobic spore-bearing bacilli, achromobacteria, and streptococci. Similar organisms, and in addition *Bacterium coli*, were also frequently found in clear fluids, only 50% of the 36 such feeds sampled proving sterile.

The following were amongst the errors in feed preparation which were often observed: absence of proper hand-washing facilities with elbow-operated taps; use of a general ward kitchen; cleansing of used bottles close to preparation of fresh feeds; faulty cleansing of bottles; incomplete contact of bottle surface with boiling water in sterilizer; handling of teats with fingers; drying of sterilized bottles with cloth; returning used bottles to milk kitchen without disinfection; leaving warm prepared feeds while awaiting distribution into individual bottles; close packing of feeds, still warm, in refrigerator; storing of unsterilized feeds at room temperature; exposure of feeds and utensils to dust; use of staff nursing sick children to make up feeds; and refrigerator breakdowns. "The most important omission, however, was failure to place responsibility for feed preparation in the hands of one person trained in the principles of sterilization and milk hygiene".

The ideal is considered to be terminal heat treatment of all feeds, but whether this method is applicable to dried-milk feeds, which are in common use in this country, is not known. From the work of American workers it is suggested that the minimum acceptable standard should be a bacterial count of fewer than 500 colonies per ml. Model milk kitchens should be set up as training centres and for trying out new devices and new techniques.

Douglas Gairdner

1911. Enuresis and Toilet Training

J. BOSTOCK and M. G. SHACKLETON. *Medical Journal of Australia* [Med. J. Aust.] 2, 110-113, July 28, 1951. 7 refs.

The relationship between domestic happiness and a satisfactory emotional attitude to breast-feeding is demonstrated statistically, together with the association that exists between a maternal dislike of breast-feeding and the development of aggressive, destructive, and

stubborn impulses in the child. However, the same direct correlation with personality deviation is not found in the genesis of enuresis. No relation between the type of breast-feeding and enuresis can be demonstrated. The method of toilet training is very important. Of 43 children subjected to a rigid and impatient regime, 26 were enuretics, while of 30 who were trained without coercion only 3 became bedwetters.

There is also a significant relationship between the welcome to the child (whether it was wanted or not by the mother) and rigidity in toilet training. It is suggested that the mother uses an intensive campaign to perfection in the child as compensation for a lack of love. In other cases the mother of a wanted baby may succumb to the wiles of the baby-trainer and institute a harsh regimen. In either case the early cleanliness of the infant is based upon fear and insecurity and thus is a habit learned under frustration. This tends to break down in the face of further frustration with the appearance of stereotypes.

The statistics given in this paper show how enuresis is to be prevented. Treatment of the existing condition consists in discovery of the causation and removal of frustration factors.

[Although no association of the type of breast-feeding with enuresis is found, it would be interesting to investigate any relation between complete lack of breast-feeding, particularly in the case of the pram-bottle-fed baby, and enuresis.]

E. H. Johnson

1912. Significance of Convulsions in Children with Purulent Meningitis

C. OUNSTED. *Lancet* [Lancet] 1, 1245-1248, June 9, 1951. 13 refs.

The author presents a study of 90 consecutive cases of purulent meningitis admitted to the children's departments of the United Oxford Hospitals between November, 1946, and March, 1950, and which received the chemotherapy appropriate to the infecting organism. A relationship seems to exist between the occurrence of fits and the outcome of the disease. Failures of treatment increase with the number of fits. Of the 53 children in whom no fits occurred, 51 were cured; of the other 37 who had had fits, only 21 were cured and in 2 of these delayed sequelae developed.

Age is clearly a factor in the aetiology of convulsions in meningitis. There were 17 children aged over 4 years, and 2 of these had fits; of the 73 children aged less than 4 years, 35 had fits. Only one of the 17 failures in this last group escaped convulsions. Thirty-seven of the 56 cured cases escaped convulsions. Of the total of 38 who escaped convulsions 37 were cured. Nearly half the failures in this group were associated with status epilepticus.

Fits occurring after admission to hospital carry the graver prognosis. The cure rate is higher in the group

treated prophylactically with phenobarbitone. The author advocates the administration of this drug in prophylaxis on a weight-for-age dosage; he also advocates lumbar puncture in every case of unexplained febrile seizure in small children. Rapid and extensive treatment of established convulsions is indicated. The drug of choice is not established, but the results of trials with intramuscular injection of sodium isoamylethyl barbiturate are promising.

The mechanism by which convulsions may lead to death or permanent cerebral damage is discussed.

Margaretha Adams

See also Microbiology, Abstract 1897.

1913. Complications of Intravenous Fluid Therapy in Children

R. McL. TODD. *Lancet [Lancet]* 1, 982-985, May 5, 1951. 3 refs.

The author performs a useful service in drawing attention to the frequency of complications of intravenous fluid therapy in children, particularly in the very young. Venous thrombosis or local wound sepsis occurred in nearly one-fifth of a series of 664 continuous intravenous drip infusions performed by the "cut-down" method, but prolonged therapy in severely debilitated infants and the use of protein hydrolysates probably contributed to this high incidence; the consequences were not serious. However, generalized septicaemia occurred in 8 cases, all but 1 being due to penicillin-resistant organisms. It is suggested that routine administration of streptomycin rather than penicillin should be adopted, but that greater attention to asepsis is paramount. Fatal homologous serum hepatitis, temporary wrist-drop, and transient overloading of the circulation also occurred, each in 1 case.

M. Baber

1914. Aqueous Dispersions of Vitamins A and D in Premature Infants. Studies with Reference to Rickets and Retrolental Fibroplasia

B. KRAMER, S. M. GORDON, H. M. BERGER, and A. E. SOBEL. *American Journal of Diseases of Children [Amer. J. Dis. Child.]* 82, 17-27, July, 1951. 1 fig., 28 refs.

In this paper are recorded the results of an investigation planned to assess the relative value of aqueous and oily preparations of vitamins A and D in the prevention of rickets and retrolental fibroplasia in premature infants.

Starting on the seventh postnatal day 65 premature infants were given oral doses of vitamin concentrates: 35 received a daily dose of an aqueous solution containing 1,200 units of vitamin D and 5,000 units of vitamin A, and the remaining 30 were given 1,260 units of vitamin D and 8,750 units of vitamin A in an oily solution. The average duration of in-patient treatment in the latter group was 39.6 days, and in the former 34.8 days. The average weight gain for both groups was the same (2 lb. 5 oz.=0.97 kg.). On the day of discharge the wrists were examined radiologically for signs of rickets and samples of blood were taken for estimation of calcium, phosphorus, and phosphatase concentration. None of the infants showed any clinical or radiological

evidence of rickets. The differences between the blood levels of phosphorus, phosphatase, and calcium-phosphorus products were not statistically significant in the two groups. Thus it is evident from these studies that with the doses used vitamin D is at least as effective in an aqueous solution as in an oily solution in the prevention of rickets in premature infants.

During one 3-year period (1943-6) all premature infants were given vitamin A in oil, and in the next 3-year period (1947-9) in an aqueous solution. Of 596 of these babies subsequently examined only 5 had developed retrolental fibroplasia, and all except one had weighed less than 3 lb. (1.36 kg.) at birth. In view of the small number of cases no conclusions can be drawn, but there was no increase in incidence of retrolental fibroplasia during the period vitamin A was being given in an aqueous solution.

Jas. M. Smellie

1915. Pneumatosis Intestinalis in the Newborn

O. A. STIENNON. *American Journal of Diseases of Children [Amer. J. Dis. Child.]* 81, 651-663, May, 1951. 2 figs., bibliography.

Two cases of pneumatosis intestinalis are reported from Ann Arbor, Michigan. The outstanding clinical features were abdominal distension and bloody, mucous stools. On x-ray examination of the abdomen radio-translucent bands outlining the involved parts of the intestines were shown; on microscopy in 1 case gas was found to be present in the wall of the colon. The aetiology is considered in detail, and the neoplastic and bacterial theories are discarded in favour of the mechanical theory. Any explanation of the cause of pneumatosis intestinalis must account for the frequent association of this condition with pyloric stenosis and ulceration, and the predilection of the gas for the mesenteric border of the intestine.

It is concluded that the condition develops in an ulcerated area of the stomach when gas is present under pressure. The gas escapes between the layers of the gastro-hepatic and hepato-duodenal ligaments to reach the root of the mesentery and from there, by following the blood vessels, it dissects through to the submucosal layer of the intestine. This may result in occlusion of the lumen of the bowel and intestinal obstruction, or by pressure on the blood vessels the mucosa may be rendered avascular. The varied x-ray appearances which may be encountered are also described.

[There is a report of a further 13 cases in infants by Mackenzie, *Pediatrics*, 1951, 7, 537.]

R. M. Todd

1916. Congenital Hypertrophic Pyloric Stenosis. Review of 320 Cases

E. C. WOOD and J. M. SMELLIE. *Lancet [Lancet]* 2, 3-7, July 7, 1951. 16 refs.

At the Birmingham Children's Hospital from 1948 to 1951, 320 infants have been treated for congenital hypertrophic pyloric stenosis. The authors describe the aetiological factors, the symptoms, and the results of treatment. They give a useful review of the recent literature about the incidence and mortality rate and note the general improvement in results, which is also evident in Birmingham.

ham. In 1939 the mortality rate was 24%; in the period 1947-9 it was 1.6%. In the authors' series the percentage of males was 79.4 and of firstborn infants 51. In 16 families one or more previous siblings were affected. In the 5 cases in binovular twins only one was affected. The average age of onset was 3.3 weeks, but a few babies had projectile vomiting from birth. In 12 cases there was bile and in 27 blood in the vomit. The average age on admission was 5.8 weeks, and 155 (49.6%) of the babies were breast-fed. A pyloric tumour was felt in 97.3% and gastric peristalsis was seen in 82%. X-ray studies were not made until recently. The authors conclude that routine use of radiological examination is unnecessary, but that time may be saved where a doubtful tumour is felt if the narrowed pyloric canal can be demonstrated as a constant shadow.

The infants are classified on a basis of weight on admission, 200 (63%) being more than 80% of expected weight, 95 (29.6%) 70 to 80%, and 23 (7%) less than 70% of expected weight. The proportion of uninterrupted recoveries in these three groups was 77%, 51.6%, and 36% respectively. Of the 29 babies weighing less than 6 lb. (2.7 kg.) on admission, 41% made uninterrupted recoveries; 2 babies under 4 lb. (1.8 kg.) died. About half of the 69 babies suffering from complicating infections on admission had otitis media.

The treatment was mainly surgical (94%). The Fredet-Rammstedt operation was performed by any one of the surgeons under local procaine with gas, oxygen, and ether, the cases being nursed in medical wards under the general care of the physician. Before operation rehydration is essential. Where there is deficiency of urinary chlorides additional saline solution is given, and when ketones are present longer pre-operative treatment is necessary. Parenteral fluid was required in 61% and intravenous therapy in 26% of cases. Infection was treated by suitable chemotherapy. Details of post-operative care are given. The breast-fed babies returned to the breast in 24 to 48 hours.

The average pre-operative stay in hospital was 1.8 days and the average total stay 14.6 days, delay in the hoped-for return home on the fifth day being due to unsatisfactory home conditions, great distance of the home from the hospital, or the occurrence of infection.

The authors kept careful note of all post-operative complications, including even the mildest. No patient was readmitted for recurrence, but a few were brought back with sepsis or gastro-enteritis. There was clinical evidence of infection in 78 cases (26%), 33 babies having wound infection, 12 otitis media, 14 relaxed stools, 9 gastro-enteritis, 7 upper respiratory infections, and 10 minor superficial infections. Since all patients were nursed in the special cubed infant section of the hospital, with scrupulous attention to barrier nursing, the blame is attached to the nutritional derangement associated with the disease. Of non-infective complications (20), vomiting, which responded readily to reduction or withholding of oral feeds, occurred in 12 cases. There were 5 deaths: one from bronchiolitis and asphyxia, one from massive post-operative haemorrhage, one from pyaemia due to infection of the intravenous wound, and one in a baby weighing 3 lb. 1 oz. (1.4 kg.) at 10 weeks

who had multiple congenital defects, including agenesis of the right kidney; the fifth death was due to Friedrichsen-Waterhouse syndrome present before operation. Twenty cases (6%) were treated medically, and in 4, after unsuccessful medical treatment, Rammstedt's operation was performed. Atropine methyl nitrate (0.1 to 0.3 mg.) in water or as a lamella half an hour before meals was used throughout, with twice-daily gastric lavage and small thickened feeds. The average stay in hospital in these cases was 22 days. No severe infective complications occurred, but those involved were older babies with less severe vomiting.

A. W. Franklin

1917. Aureomycin and Chloramphenicol in Infantile Diarrhoea

R. A. SHANKS. *British Medical Journal* [Brit. med. J.] 2, 272-275, Aug. 4, 1951. 9 refs.

Aureomycin or chloramphenicol was given to 92 children suffering from infantile diarrhoea of non-specific origin in their first year of life. Controls were given penicillin and/or sulphonamides. Of the total, 17 children received aureomycin orally in doses of 25 mg. per kg. of body weight a day in 3 or 4 divided doses for 7 days, and 30 children were given chloramphenicol in doses of 150 mg. per kg. of body weight a day in 4-hourly doses for 7 to 10 days. The three methods of treatment did not result in any significant difference in the mortality and the average duration of stay in hospital. It seems that the various antibacterial substances have only a limited value in the treatment of infantile diarrhoea and that their ineffectiveness suggests that this disease has a non-bacterial causation.

Franz Heimann

1918. Homologous Serum Hepatitis in a Very Young Infant

J. TROY. *Journal of the Indiana State Medical Association* [J. Indiana med. Ass.] 44 756-757, Aug., 1951. 4 refs.

See also Radiology, Abstract 1852.

1919. Sinobronchitis in Infants and Children

W. C. PRICE. *Journal of Pediatrics* [J. Pediat.] 38, 590-596, May, 1951. 14 refs.

The author stresses the frequent association of sinusitis and lower respiratory tract infection. Sino-bronchitis is defined as involvement of the sinus membranes by an infective process of sufficient intensity to have implanted itself likewise upon the bronchial mucosa either directly (by means of contiguous extension or post-nasal secretion) or indirectly (by lymphatic spread). Of the 384 children who were examined 126 showed evidence of sino-bronchial disease. More advanced disease was found among children under 9 years of age. It was five times as frequent among children suffering from chronic respiratory disease as it was among children with non-respiratory illnesses.

A description is given of the x-ray appearances of the chest and sinuses of the children suffering from sino-bronchitis. The aetiology, complications, and symptoms of the disease are discussed.

B. S. P. Gurney

1920. A Treatment Program for Chronic Childhood Sinobronchitis

W. C. PRICE and V. B. BINNS. *Journal of Pediatrics* [J. Pediat.] 38, 597-601, May, 1951. 7 refs.

The authors claim to have established an improved treatment for chronic sino-bronchitis in children. It is based on the theory of Hansel that antibiotic therapy alone cannot prevent the exacerbation of chronic sinusitis, but must be supplemented with anti-allergic measures to control the allergic response of the sino-bronchial mucosa to bacterial protein.

The anti-histaminic compound used was "syrup of histadyl", and the best results were obtained with the following treatment: intramuscular procaine penicillin in one daily dose of 300,000 units; 4 aerosol penicillin inhalations daily in doses varying from 50,000 to 100,000 units; histadyl 4 times a day in doses varying from 15 to 50 mg. according to age, which varied from 18 months to 15 years; nasal drops of penicillin in "paredrine" given immediately before each inhalation of penicillin aerosol. The results were excellent in 13 cases, good in 5, and fair in 1; in 1 case there was no improvement.

B. S. P. Gurney

1921. Sympathetic Neuroblastoma in Infancy. A Clinical Study. (Neuroblastoma simpatico en la infancia. Estudio clinico)

J. JORDÁN RODRÍGUEZ. *Revista Cubana de Pediatría* [Rev. cubana Pediat.] 23, 257-285, May, 1951. 18 figs., 21 refs.

The author considers that though reports of cases of neuroblastoma in infancy are relatively rare in the Cuban literature, this does not represent a true scarcity of cases. He records the clinical and pathological findings in 4 cases seen personally. After a brief review of the embryology and of the relationship between sympathoblastoma (neuroblastoma) and other tumours originating in neural-crest elements, there is an account of cases described in the literature. The typical clinical manifestations of the tumour are then described: the symptoms include extreme anorexia, asthenia, pallor, and loss of weight, while the physical signs are those of a retroperitoneal tumour with or without metastases in liver or bone. A blood count usually shows severe hypoplastic anaemia and sometimes thrombocytopenia, and irregular syncytial groups of tumour cells may be found on marrow puncture. Pyelography, perirenal insufflation, and direct lumbar aortography may help in delimiting the primary tumour mass, and radiological examination of the long bones may reveal secondary deposits, often symmetrically placed. In the differential diagnosis of cases with a palpable abdominal tumour Wilms's tumour, lymphosarcoma, tumours of the adrenal cortex, and hydronephrosis must be excluded, while in cases with metastases the conditions to be differentiated include: (1) in the Hutchison type, chloroma, Hand-Schüller-Christian syndrome, osteosarcoma, and tuberculous osteitis of the cranium; and (2) in the Pepper type, haemangio-endothelioma of the liver and other causes of infantile hepatomegaly. While admitting that treatment is usually unsatisfactory, the author recom-

mends surgical extirpation when possible, and deep x-ray therapy.

[As is now almost invariable in foreign literature, Hutchison's name is spelt "Hutchinson".]

J. B. Stanton

1922. Encephalographic Observations in Little's Disease. (Osservazioni encefalografiche sul morbo di Little)

C. STICCA. *Lattante* [Lattante] 22, 257-268, May, 1951. 10 figs., 13 refs

In this paper the older term of "Little's disease" is used as embracing all forms of congenital spastic paralysis of children. Previous attempts to demonstrate encephalographic changes occurring in this disease are discussed. These are inconclusive, and for the present study a survey of the differences in size of the cerebral ventricles in normal children was made as a preliminary necessity. Among the abnormal cases, 51 in number, the lateral ventricles appeared abnormally enlarged in 31 cases; in 6 cases there was a clearly hydrocephalic dilatation, while the remainder had ventricular enlargement that was considered pathological. Enlargement is usually to be seen, if at all, in the fronto-occipital projection; in one case the third ventricle was enlarged. Definite ventricular asymmetry was found in 21 cases. In only 4 cases could dilatation of the sulci be seen, and it was regarded as significant only in 3 of these, in which there was an accompanying ventricular enlargement. Typical radiographs are reproduced.

The author concludes that there is no characteristic encephalographic picture in Little's disease, but in a considerable proportion of cases there is a slight ventricular dilatation.

Donald McDonald

1923. Blood Incompatibility between Mother and Child in Etiology of Mental Deficiency

I. ZWERLING, H. GOLD, G. A. JERVIS, and V. GINSBERG. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 82, 7-13, July, 1951. 12 refs.

To study the possible relation between blood incompatibility and the occurrence of mental deficiency the authors determined the blood groups of 495 mentally defective children and their mothers. In this series the percentage of idiots and imbeciles was considerably greater than would be the case in a general cross-section of the population. The cases were divided into four groups: (1) cause unknown; (2) cause known—such as trauma, definite heredity, encephalitis, and endocrine disorder; (3) cause uncertain; (4) mongols. The antigens, A, B, C, c, D, and E were determined. Patients with erythroblastosis and kernicterus were not included.

No statistically significant difference was found in the distribution compared with the expected numbers. However, among incompatible D-factor pairs, when first-born children and negroes were excluded, a higher number belonged to Group 1 than was expected, the difference approaching statistical significance. The results suggested that a few cases may be due to isoimmunization with the D factor, even without the existence of haemolytic disease. The histories of 2 such cases are outlined.

E. H. Johnson

1924. Evidence of Adrenal Cortical Function in Pink Disease

D. B. CHEEK, B. S. HETZEL, and D. C. HINE. *Medical Journal of Australia [Med. J. Aust.]* 2, 6-9, July 7, 1951. 21 refs.

The first author and co-workers previously demonstrated a disturbance of electrolyte and water metabolism in pink disease. The present authors report an investigation into the activity of the adrenal cortex in 10 cases of pink disease. The children affected had normal urinary glucocorticoid excretion, significant elevation of the neutral 17-ketosteroid excretion, and a normal response of the circulating eosinophil cells to 0.2 mg. of adrenaline injected subcutaneously. The authors conclude that in pink disease there is no simple hypofunction of the adrenal cortex, but that there may be a fractional disturbance of the "sodium and water hormone", or that the sodium depletion may be due to extra-adrenal causes.

R. S. Illingworth

1925. Hypothyroidism in Childhood

F. BRAID. *British Medical Journal [Brit. med. J.]* 1, 1169-1176, May 26, 1951. 8 figs., 22 refs.

The author distinguishes three types of hypothyroidism among the children he has observed: congenital hypothyroidism (24 cases), post-infective hypothyroidism (6 cases), and endemic cretinism (9 cases). The congenital condition is due either to a developmental defect or to transplacental infection of the thyroid. 3 children dying at 3 to 3½ months had no thyroid gland, and it was very small in one child dying at 8 months; in a premature child, whose mother had recently had influenza, the thyroid was inflamed and fibrotic, with few follicles and pale, vacuolated colloid. Such a congenital defect in a surviving child might well cause deficiency as thyroxine needs increased later in life. In patients in the second group onset of symptoms was often associated with some acute infection such as measles or pneumonia and the thyroid changes were probably similar. The dangers of thiouracil treatment affecting the foetus must be borne in mind; the drug passes through the placenta and also into the milk. Endemic cretinism is usually the product of generations of goitrous conditions and is gradually disappearing.

Congenital hypothyroidism can be recognized as early as the seventh week, and 5 children of this group were diagnosed before the fourth month. Commonest symptoms are the appearance of supraclavicular pads, "jaundice" (which is actually carotenaemia caused by failure of carotene to be converted into vitamin A in the absence of thyroxine), slow feeding, lethargy, anaemia, umbilical hernia or abdominal distension, constipation, and later the more typical adult hypothyroid symptoms: myxoedema, dry skin, and hoarse voice. Post-infective hypothyroidism results in the cessation of previously normal development and, though hypothyroid symptoms are not so pronounced, inadequate teething, supraclavicular pads, solemn expression, physical inactivity, and mental dullness are common. Cases of endemic cretinism usually come under observation later with a history of apathy, late teething, walking, and talking, and

gruffness of voice. Myxoedematous symptoms are not marked, but stunting of growth is considerable and goitre, spasticity of the limbs, and low intelligence are common findings.

Diagnosis is based on changes in the skeleton, blood cholesterol level, and electrocardiogram, and the response of these to thyroid treatment. Radiographs of the skeleton show arrested growth characterized by the increased density of provisional zones of calcification and delayed appearance of ossification centres. Thyroid treatment produces growth within a few weeks and fresh ossification centres appear within some months. The irregularity of ossification indicates cartilage disturbance and the irregularity increases if treatment is delayed. Deformity of the head and neck of the femur accounts for the waddling gait. Blood cholesterol levels vary in children, but values above 200 mg. per 100 ml. suggest hypothyroidism. In the present cases values ranged from 116 mg. to 479 mg. per 100 ml. The reduction produced by thyroid medication is pronounced and is a better index of the adequacy of treatment than is the skeletal picture.

Changes in heart size or rate are uncommon, but cyanosis of the extremities indicates a sluggish circulation and there are characteristic changes in the electrocardiogram: a low-voltage curve with flattened P and T waves and occasional lengthening of the P-R and Q-T intervals. Restoration of a normal electrocardiogram is the simplest check on treatment. The usual anaemia is normocytic, orthochromic, and mild; it does not respond to iron, but is improved by thyroid treatment after a temporary apparent worsening caused by the restoration of plasma volume. Muscle atony is common and may persist despite treatment and resemble familial or pseudo-hypertrophic muscular dystrophy. The gastro-intestinal symptoms (lack of appetite, slow feeding, and constipation) may be reversed to diarrhoea by inadequate treatment or may persist, with dilatation of the colon. Blood phosphatase levels tend to be low and there is evidence of calcium retention in the bone density and diffuse calcinosis of soft tissues found in some cases.

Untreated cases are particularly sensitive to thyroid treatment, which must be started with low doses (8 mg. daily) and must be carefully controlled during the first few months. Loss of weight, diarrhoea, and rise in temperature are all indications of overdosage. Later control can be exercised at longer intervals, but must be continued to ensure that increasing bodily needs are met with adequate dosage. The results of treatment are tabulated and analysed. Early treatment is most important in the congenital cases, development during the first few months being particularly rapid and fundamental.

Almost all the author's congenital and post-infective cases regained normal height and intelligence. Results in the group of endemic cretins were poor. Increase in growth was slow and the patient was always sub-normal both in height and intelligence. The relations between intelligence and type of case, type of treatment, and final result are obscure and the literature on this point is discussed.

Peter C. Williams

Medicine: General

1926. Delayed Effects of Ultraviolet Burns in Man

M. L. THOMSON. *Lancet* [Lancet] 1, 1347-1348, June 23, 1951. 2 figs., 6 refs.

This is a report on 2 healthy men who were undergoing standard tests in a climatic chamber at the Tropical Research Unit, Singapore: one was accidentally exposed to sunburn and the other was given ultraviolet irradiation. In both instances severe erythema followed within a few hours, accompanied by giddiness and faintness. Both subjects were unable to work in a hot environment on the next day, though they were able to do the same work in the same environment on the previous and following days. At the same time their pulse rate and rectal temperature rose higher than usual, and one of the subjects sweated less. A fortnight after the first exposure the latter subject was again irradiated, and on the next day, while working in the hot room, he again sweated less and had a higher pulse rate and rectal temperature than usual.

The author's suggestion is that the acute erythema and blistering of sunburn may cause a temporary reduction in sweat rate and that this may predispose to heat exhaustion, but he implies that graduated sunbathing need not be avoided in the Tropics.

The paper also contains a discussion of skin changes after sunburn, and the case report of a man who became badly burnt and blistered after sunbathing on a beach. No experiments were carried out on this third subject, though it was found that the composition of the sudaminous contents of vesicles on his skin was similar to that of sweat.

E. M. Glaser

1927. Changes in Sweating after Prickly Heat

W. S. S. LADELL. *British Medical Journal* [Brit. med. J.] 1, 1358-1360, June 16, 1951. 2 figs., 16 refs.

The case is reported from the Colonial Medical Research Committee's Laboratory for Hot Climate Physiology at Lagos, Nigeria, of a patient who developed severe prickly heat soon after he joined the laboratory staff and who was treated with salicylic acid and perchloride of mercury in spirit, as well as with olive oil after his bath. The condition cleared up in about 1 month and the patient continued to live in the hot, humid climate of Nigeria and to work as an observer during experiments which were carried out in very hot climatic chambers.

Some 5 months later he was found to respond to a given combination of work and environmental heat by losing more water and chlorides in his sweat and having a higher rectal temperature than he did before he had had prickly heat and before he could have been fully acclimatized from the point of view of sweating. The author suggests that there may have been some change in the sweat glands as a result of prickly heat, or that the patient suffered from a "disease of adaptation" as described by

Selye (*Brit. med. J.*, 1950, 1, 1383). The author's own classical observations, which have been more recently confirmed in America—namely, that it is the adrenal cortex which controls sweating—add weight to this argument (Ladell, *J. Physiol.*, 1945, 104, 13).

E. M. Glaser

1928. Prevention and Treatment of Travel Sickness with Promethazine Chlorotheophyllinate

J. HARPER. *Lancet* [Lancet] 1, 1141-1144, May 26, 1951. 21 refs.

In a large Atlantic liner passengers who sought treatment for sea-sickness were divided into a prophylactic and a therapeutic group. The former group included those who came for advice before or soon after sailing, those who came at the threatened approach of rough weather, and those who came in the initial stages of their reaction to the ship's motion, when their symptoms were confined to malaise. Most of the therapeutic group were in the later stages of sea-sickness. For prophylaxis one 25-mg. tablet of promethazine chlorotheophyllinate ("avomine") was given each evening for 3 days, and for treatment two 25-mg. tablets on the first day and a third tablet on the evening of the second day.

Rigid assessment of a sea-sickness remedy in peacetime North Atlantic travel conditions is unsatisfactory. Personal follow-up of a large number of cases is impracticable when the voyage takes only 5 or 6 days. Regular reporting by cabin staff and a check of those passengers still in their cabins on later days were used to estimate probable failures. The use of an inert substance as a control is unjustifiable in the case of fare-paying passengers. Of the 50 passengers given prophylactic treatment 46 did not suffer from sea-sickness. Of 274 passengers in the therapeutic group 239 were treated successfully with 3 tablets of 25 mg. each. The author concludes that avomine is a safe and effective remedy for sea-sickness; its side-effects in the above dosage are insignificant, and treatment does not seem to interfere with the normal mechanism of adaption to the disturbing motion.

[This and other "pioneer" studies have shown that many antihistamine drugs are effective in sea-sickness. These include "amosyt", "avomine", diphenhydramine, "dramamine", "lergigan", and promethazine hydrochloride. The need is for a comparative study of these antihistaminics, with and without hyoscine, to determine the most suitable treatment. It is unfortunate that this otherwise excellent article should be marred by the confusion of "lertigon", which is a histamine azo-protein, with "lergigan", which is the hydrochloride of a phenothiazine base, and that "unsuccessful" should have been substituted for "successful" in the tabulated results.]

R. Hodgkinson

1929. Experiences with ACTH and Cortisone in the Treatment of Asthma and Eczema in Infancy and Childhood

J. GLASER, S. C. SIEGEL, J. D. GOLDSTEIN, and R. S. MELTZER. *Annals of Allergy* [Ann. Allergy] 9, 292-298, May-June, 1951. 6 refs.

Ten asthmatic children and 3 children suffering from eczema, 5 of them younger than 2 years, were studied, first in hospital and some of them later as out-patients. Blood chemistry and cytology were studied in detail [the results are not given]. Both ACTH and cortisone caused a marked improvement, but a relapse followed when administration was stopped. The longest remission was 4 months. The dosage required was proportionally higher than in adults; it varied according to the severity of the disease. The immediate-wheal type of skin reaction was not influenced by the treatment.

H. Herxheimer

1930. The Use of ACTH in the Treatment of Ambulatory Asthmatic Patients

E. A. BROWN, L. A. FOX, C. NOBILI, P. P. NORMAN, R. C. NORTON, and S. RUBY. *Annals of Allergy* [Ann. Allergy] 9, 459-464, July-Aug., 1951.

A series of 30 patients with asthma and 10 with allergic dermatitis were treated as out-patients with ACTH in 6- to 12-hourly injections. As soon as a good response was obtained the dose was gradually reduced to the minimum required for maintenance. In the self-limiting cases of dermatitis ACTH could be omitted without the disease recurring; in asthma this was not possible, but in some cases treatment was continued for 10 months without difficulty. It is stated that ACTH is especially indicated in such cases in which remissions had previously occurred, in self-limiting conditions, and in the severe asthmatic state. It cannot replace other anti-allergic treatment. Four illustrative cases are described in detail.

H. Herxheimer

1931. Acetylcholine and Cholinesterase in the Blood of Patients Suffering with Bronchial Asthma

H. H. SCUDAMORE, L. J. VORHAUS, and R. M. KARK. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 37, 860-866, June, 1951. 2 figs., 26 refs.

The authors compared the blood levels of acetylcholine and cholinesterase in 14 healthy men and women and 8 with bronchial asthma. The acetylcholine in the serum was determined by the method of Wait, using the isolated heart of the clam. The plasma and erythrocyte cholinesterase were measured electrometrically by the method of Michel. The mean value for acetylcholine-like substances in the serum of healthy individuals was 1.28 ± 1.20 μg . per 100 ml. The values ranged from 0.32 to 4.80 μg . per 100 ml. of serum. Corresponding investigations on 8 patients ill with asthma showed a mean serum acetylcholine level of 3.97 ± 1.44 μg . per 100 ml. with a variation between 2.5 and 6.4 μg . per 100 ml. There was therefore an appreciable increase in the acetylcholine levels in the asthmatic group.

It was observed that there did not appear to be any correlation between the severity of the asthma and the

acetylcholine level. In one patient the blood levels of acetylcholine and cholinesterase at the peak of an attack of asthma and 50 minutes after the administration of adrenaline, when most of the symptoms had subsided, showed a difference which was probably not significant. The cholinesterase figures failed to show any appreciable difference in the plasma or erythrocytes of healthy individuals and asthmatics. The authors point out that there is need for further studies of autonomic nervous mechanisms in asthmatic subjects.

R. S. Bruce Pearson

METABOLIC DISORDERS

1932. The Treatment of Obesity with an Anorexigenic Drug

E. ROBERTS. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 1324-1330, June, 1951. 2 figs., 4 refs.

A total of 60 females and 4 males were treated for obesity by a regimen of diet restriction to between 1,000 and 1,800 Calories a day combined with "dexamyl", which is a mixture of "dexedrine" (D-amphetamine sulphate) and "amytal" (amylobarbitonum). For those weighing over 160 lb. (72.5 kg.) the starting dose was equivalent to 2.5 mg. of dexedrine three times a day and the optimal dose was double this.

During 3 months' study there was satisfactory loss of weight in 59 of the patients; only 4 failed to lose weight. (The course of treatment was not completed in one patient.) The average weight loss was 19 lb. (8.6 kg.) in 3 months for those less than 69%, and 26 lb. (11.8 kg.) for those more than 70%, over normal weight. Weight returned to normal within 3 months in 14 cases, and 28 subjects were within 19% of normal. Side-effects, such as sleeplessness, did not occur.

Among the series investigated were 10 diabetic patients, and these were subjected to a separate analysis. Their average loss of weight was 7.6 lb. (3.45 kg.) in the first month and 16.7 lb. (7.57 kg.) in 3 months. Insulin requirement was reduced as weight fell. The author concludes that dexamyl may be of definite benefit in overweight diabetics. In 7 hypertensive patients no rise in blood pressure occurred, but similar weight reduction was achieved.

C. L. Cope

1933. A Clinical Study of Malnutrition in Japanese Prisoners of War

M. A. SCHNITKER, P. E. MATTMAN, and T. L. BLISS. *Annals of Internal Medicine* [Ann. intern. Med.] 35, 69-96, July, 1951. 5 figs., 43 refs.

After VJ Day—Sept. 2, 1945—Japanese troops began to surrender by the thousand. By early October 80,000 had been confined in New Bilibid Prison and the hospital was called upon to deal with 5,700 sick, the majority suffering from malnutrition. As circumstances would not permit a detailed study of this material, it was decided to make a purely clinical study, during the 6 weeks available, of a small group from among those most severely starved—24 in number: "12 with massive edema (so-called 'wet' beriberi) and 12 with no edema (so-called

'dry' beriberi)". [These terms were used as a matter of convenience, as the authors state elsewhere that they had no previous experience of these conditions and the local Japanese doctors did not recognize them as being forms of beriberi.]

The patients were placed in a special ward and given ordinary medical care together with a diet of 3,400 Calories; this included 12 oz. (340 g.) of meat, citrus fruit juices, yeast tablets, 10 mg. aneurin chloride, and 15 gr. (1 g.) of ferrous oxide. They were all males ranging in age from 21 to 49 years. The history in each case revealed a period of starvation of between 5 and 6 months, the diet being roughly estimated at 1,000 Calories. Three-fourths of the patients had had malaria, two-thirds diarrhoea. There had been considerable loss of weight and appetite, and marked weakness was universal. Oedema occurred in the cases of "dry" as well as in those of "wet" beriberi, and was associated with palpitation, dyspnoea, post-prandial epigastric fullness, and oliguria. Only 2 in each group complained of mild disturbances of vision, none of night-blindness; one patient with "dry" and 8 with "wet" beriberi complained of some diminution of hearing; 5 in the "dry" and one in the "wet" group gave a history of sore tongue; 2 in each group had cheilitis. Five in the "wet" and 8 in the "dry" group gave a history of subjective neurological symptoms—tingling and numbness—in the lower limbs, but no instance of the "burning-foot syndrome" was encountered. In the "wet" group the oedema was marked in the lower limbs and abdomen and was associated with ascites, and in a third of the cases the genitalia were involved; all but 3 patients had pleural effusion.

"The patients in the dry group looked like skin and bones"; the skin was dry, loose, and atrophic. In half of each group hyperkeratotic "goose-flesh" skin was noted, but this, though suggesting a vitamin-A deficiency, cleared up with soap and water after a few days. A peculiar uniform orange discoloration of the nails of the fingers and toes was seen in 3 cases. No pellagrous signs were observed. Cardiac changes were minimal; in none were there signs of cardiac failure as usually seen in beriberi. The blood pressure in the "wet" cases was normal, in the "dry" cases subnormal. The lungs and abdomen were normal apart from ascites and pleural effusion. Neurological findings were also minimal, and consisted of only minor sensory changes in a few cases. There was no paralysis, neither was there loss of deep tendon reflexes, though the responses were variable; in none of the patients was a positive Romberg or Babinski sign elicited. The necropsy findings in 5 cases are included.

The authors draw the following conclusions: "(1) An analysis of the findings does not support our early assumption that these were cases of wet and dry beriberi. (2) There was no evidence clinically or pathologically of beriberi heart disease or other organic heart disease, nephritis, or venous or lymphatic obstruction to account for the edema. (3) A number of the patients, both wet and dry, exhibited increasing edema with an intercurrent attack of malaria. On the other hand, control of the malarial attack was frequently associated with diuresis

and loss of edema fluid. The reasons for this were not apparent. (4) The clinical picture was one of nutritional hypoproteinemia, with a spruelike syndrome manifested by marked alterations of serum proteins, with or without edema, with glossitis, diarrhoea and marked wasting. These changes were attributed to inadequate food intake, probably with secondary alterations in the gastrointestinal tract which prevented the proper absorption and assimilation of foodstuffs. (5) With nearly all of the abnormal findings so similar in the two groups, we are unable to explain why some should have had such massive edema and the others none. Possibly differences in sodium intake prior to capture, or in sodium clearance, may suggest an answer."

[It is not possible to include the results of all the laboratory and special investigations, for details of which the original article should be consulted.]

H. S. Stannus

1934. **The Effect of Citrovorum Factor ("Leucovorin") on the Blood Picture and Clinical and Neurological Manifestations of Tropical Sprue.** (El efecto del factor citrovorum (leucovorin) sobre el cuadro hematológico y las manifestaciones clínicas y neurológicas del esпру tropical)

R. M. SUAREZ, E. C. MARTINEZ, R. M. SUAREZ, JR., and A. E. LATORRE. *Boletín de la Asociación Médica de Puerto Rico [Bol. Asoc. méd. P. Rico]* 43, 319-326, June, 1951. 2 figs., 10 refs.

Two cases of sprue with macrocytic anaemia were treated with *Leuconostoc citrovorum* growth factor. The first patient was given 1 ml. (3 mg. or 20,000,000 units) intramuscularly for 5 days. A 25% reticulocytosis followed on the 7th day, the general symptoms abated, and the haemoglobin level rose, but a marrow biopsy still revealed megaloblastic erythropoiesis after 3 weeks. The second patient, who had neurological signs indicating posterior-column involvement, received 1 ml. intramuscularly for 26 days with more rapid haematological response. The reticulocyte count rose to 35% on the 8th day and haemoglobin level from 8.4 g. to 11.4 g. per 100 ml. after 26 days. Some posterior-column sensation returned, but not the tendon reflexes.

The authors also discuss the relationship of vitamin B₁₂ to folic acid and the citrovorum factor.

K. Gurling

1935. **Aminoacid Metabolism in Cystinuria**

C. E. DENT and G. A. ROSE. *Quarterly Journal of Medicine [Quart. J. Med.]* 20, 205-219, July, 1951. 2 figs., 26 refs.

In this investigation the urine of 15 adults who had the typical form of cystinuria with a strongly positive cyanide-nitroprusside urine reaction was analysed for amino-acids by paper chromatography. In all the cases the urinary excretion of cystine was grossly excessive (estimated to be approximately 1 g. during 24 hours, or 10 to 20 times as great as normal) and, in addition, the urinary excretion of lysine was abnormally high and that of arginine nearly always increased; "fast-arginine" was found intermittently in one case. The excretion of other

amino-acids was within the normal range, and cadaverine and putrescine were not found. The pattern of excretion of amino-acids was similar in all cases, and was fairly constant during periods of investigation up to 4 years. In 7 of the 15 cases the plasma was analysed for amino-acids by paper chromatography; the concentrations of all the detectable amino-acids were judged to be normal, so far as could be estimated by visual comparison of the colour strengths with ninhydrin, except in one patient whose plasma sometimes contained an abnormal concentration of "fast-arginine". In 2 cases the concentrations of cystine in the plasma were also determined by microbiological assay and were found to be normal.

Of the 15 patients, 8 had had renal stones or renal colic, and 5 were close relatives of one or more of these 8 patients; all the patients were in normal health in other respects.

It is concluded that "the immediate cause of the grossly excessive excretion of cystine, lysine, and arginine in the urine is a low renal threshold, presumably due to a defective capacity of the renal tubules to reabsorb these substances". This is in contradistinction to the view sometimes held that the condition is due to an error of amino-acid metabolism in the body tissues. The type of cystinuria studied in the present investigation can readily be distinguished by the method of paper chromatography from gross amino-aciduria, which is usually associated with serious organic disease.

Joseph Parness

1936. Whipple's Intestinal Lipodystrophy: its Relationship to the Rheumatic State

J. C. PETERSON and R. H. KAMPMEIER. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **221**, 543-560, May, 1951. 4 figs., 27 refs.

The authors describe 4 cases of Whipple's intestinal lipodystrophy which were treated in the Departments of Pediatrics and Medicine, Vanderbilt University School of Medicine, Nashville, Tenn. Clinical and laboratory findings are described in detail for each case. The diagnosis was confirmed by laparotomy and biopsy or at necropsy. Two of the patients were middle-aged men, one was a boy of 11 and one a girl of 13½ years. The 2 adult patients had had symptoms suggesting rheumatoid arthritis. The female patient had signs of disseminated lupus erythematosus in addition to Whipple's disease. Cortisone was used in the treatment of one patient, but apparently no benefit resulted. [Unfortunately details of cortisone therapy are not given.] Death occurred in 3 patients, and detailed necropsy findings are given for 2 of them.

The authors then analyse 26 cases from the literature, these cases being the only ones they can accept as genuine examples of Whipple's disease. The age and sex, symptomatology, and radiological and laboratory findings in these cases are tabulated. The authors point out the frequent association of arthritis, serositis, and endocarditis with Whipple's disease, and note that with one exception the various theories put forward to explain the pathogenesis of the disease do not take this fact into account. The exception is the suggestion by

Black-Schaffer and his associates (*Arch. intern. Med.*, 1950, **85**, 91) that the disease may be a sequel to a systemic illness characterized by inflammation of the serous membranes. The authors put forward the view that Whipple's disease should be regarded as a manifestation of the "rheumatic state" and another example of collagen disease.

C. E. Quin

See also Genetics, Abstract 1758.

DIABETES

1937. NPH Insulin: its Comparison with Previous Insulin Regimens

H. M. BAGANZ, S. C. CARFAGNO, B. Y. COWAN, and E. S. DILLON. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **222**, 1-6, July, 1951. 1 fig., 13 refs.

The authors present a serious and good study of 41 cases in which the new NPH insulin, which contains under half the protamine content of protamine zinc insulin (P.Z.I.), is carefully compared with P.Z.I., alone or with soluble insulin. It gives NPH very full marks. [It is, however, a study of not very severe cases, and it is well known that such cases do well on a moderate dose or doses of any sort of insulin. A study of the really severe case called "labile or brittle" was not undertaken, and such, in the abstracter's opinion, is the only true test of the strength and time action of any insulin. So we must wait, in spite of good impressions from various American centres, to decide whether NPH would be a useful addition to the *British Pharmacopoeia*.]

R. D. Lawrence

1938. Effect of Insulin Injections Repeated at Brief Intervals

M. SOMOGYI. *Endocrinology* [Endocrinology] **47**, 436-442, Dec., 1950. 4 figs., 4 refs.

Small doses of insulin (2.5 to 4 units) were injected intravenously into normal persons at short intervals (35 to 45 minutes) so that the blood sugar concentration was still depressed by the preceding injection when the next one was given. Under these circumstances the absolute decrease in blood sugar concentration produced by the later injections is never as great as that produced by the initial one and may become progressively less and eventually almost *nil*. This is the reverse of the Staub effect, in which successive doses of glucose produce a diminishing rise in the blood sugar concentration.

The effect is explained as being due to the mobilization of the anti-insulin forces of the body, presumably those from the adrenal and pituitary glands. Thus each successive injection has to overcome increased antagonism, and despite the rising quantity of insulin in the body (for each dose is given while part of the active insulin from the preceding dose is still present in the circulation) the total response decreases. The decrease is not, however, observed unless the initial dose of insulin depresses the blood sugar concentration below 60 mg. per 100 ml., which appears to be a critical level for pro-

voking the antagonistic mechanisms. This may be related to the observation of Cannon, McIver, and Bliss (*Amer. J. Physiol.*, 1924, 69, 46) that it is just this blood sugar concentration (allowing for differences of method) that elicits a measurable increase of adrenaline secretion in rabbits.

Peter C. Williams

1939. Lymphocytic Response of Diabetic Patients to Administration of Glucose and Insulin

S. S. LAZARUS, B. W. VOLK, M. JACOBI, W. R. SLADE, and M. ZYMARIS. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] 21, 436-443, May, 1951. 2 figs., 34 refs.

The authors, in a communication from the Jewish Sanitarium and Hospital for Chronic Diseases, New York, describe a novel method for differentiating types of diabetes mellitus. In normal persons administration of glucose orally or intravenously is followed by a reduction in the absolute lymphocyte count; in patients with Addison's disease and in adrenalectomized animals this reaction does not occur. A moderate hypoglycaemia is stated to give rise to an increase in the lymphocyte count in normal persons, and these responses are believed to depend on the integrity of the pituitary-adrenal mechanism.

To 22 fasting diabetic patients who had not received insulin for 48 hours 25 g. of glucose in a 50% solution was given intravenously. Capillary blood samples for glucose determination were taken at 30, 60, 120, and 180 minutes after administration of the glucose, and at the same intervals duplicate blood specimens were taken for total leucocyte counts. The absolute lymphocyte value was estimated by the method of Elmadjian and Pincus.

In 11 of the 22 patients there was a decline in the absolute lymphocyte count similar to that observed in normal persons; in the other 11 patients the results were variable, 7 showing a lymphocyte increase and the remaining 4 equivocal results. The authors suggest that in the 11 diabetics in whom there was a decline in the lymphocyte count there was no primary pituitary disorder. Of these patients 5 gave a history of "liver disease" which may have been the underlying cause of the diabetes. In the remaining 6 patients of this group the basic factor may have been a primary insulin deficiency. Among the 11 diabetics in whom there was failure of lymphocyte depression, there were 7 with arteriosclerosis or hypertensive cardiovascular disease, thought to be due to a pituitary-adrenal dysfunction.

I. McLean-Baird

1940. A Comparison of Blood-sugar and Urine-sugar Determinations for the Detection of Diabetes

D. HARTING and B. GLENN. *New England Journal of Medicine* [*New Engl. J. Med.*] 245, 48-54, July 12, 1951. 7 refs.

In this paper from Brookline, Massachusetts, the authors compare the relative merits of blood sugar estimations and urine testing in the detection of early diabetes. Capillary blood sugar estimation by the Folin and Wu method, and urine testing by the bismuth oxy-

chloride method and also Benedict's test, were carried out on 3,186 persons over 25 years of age, none of whom were previously known to be diabetics.

The procedure consisted of an initial blood sugar and urine test on first examination. The samples of blood for sugar estimation were classified according to the time they were taken after a meal, and (arbitrarily) patients with the highest 10% of readings were requested to re-attend (for example, those with a fasting blood sugar of 130 mg. per 100 ml. or higher). Those with more than a trace of sugar in the urine were also re-examined. It was not found helpful to re-examine those patients with a trace of glycosuria and a normal blood sugar level, as only one diabetic was detected among 139 persons in this category.

Among the 3,186 subjects examined 71 new cases of diabetes were found. If the urine test alone had been relied on, those subjects with more than a trace of glycosuria returning for re-examination, then only 40 of the 71 new diabetics would have been discovered. If only the blood sugar test had been used, 58 of the 71 new diabetics would have been found.

The authors conclude that blood sugar estimations are more sensitive than urine testing in the detection of diabetes, particularly the mild type of the disease. They also point out that the lower the "screening" blood sugar levels, the less sensitive the test becomes and the more work is entailed for the detection of fewer diabetics.

I. McLean-Baird

1941. The Relation of Hyperplastic Arteriosclerosis to Diabetes Mellitus

E. MOSCHCOWITZ. *Annals of Internal Medicine* [*Ann. intern. Med.*] 34, 1137-1162, May, 1951. 6 figs., bibliography.

The main contention of this paper from Mount Sinai Hospital, New York, is that arteriosclerosis, far from being a complication of diabetes mellitus, is one of its causes, especially in those over 40. In a series of necropsies on 130 diabetics, 103 patients with essential hypertension, 66 with peptic ulcer, and 103 with carcinoma, arteriosclerosis of the pulmonary artery was no commoner in the diabetic subjects than in the others. The difference is stressed between atherosclerosis and hyperplastic arteriosclerosis, the latter being largely the result of hypertension. A considerable proportion of elderly diabetics have had antecedent hypertension, and this the author considers to account for the increased incidence of arteriosclerosis in diabetics above and beyond that due to old age.

Gangrene found in diabetics is the result of atherosclerosis which follows an upset in the cholesterol metabolism. The hyalinization of islets in the pancreas is the result also of hypertension, and is analogous to fibrosis found in the lung, kidney, or liver in diseases where the arterioles are sclerosed and the process has spread to the capillaries. Islet hyalinization is not common owing to the threefold arterial supply of the pancreas.

G. S. Crockett

See also Pathology, Abstract 1865.

Cardiovascular Disorders

1942. The Effect of Priscol on the Peripheral Venous Pressure

K. BRAUN and C. H. FRYD. *British Heart Journal* [Brit. Heart J.] 13, 294-300, July, 1951. 1 fig., 15 refs.

The effect of tolazoline was observed upon the heart rate, arterial pressure, and venous pressure in 22 patients. Venous pressure was measured manometrically with a needle in the antecubital vein. The maximum effect of 10 mg. of the drug occurred 3 to 8 minutes after intravenous injection and passed off completely in 20 minutes.

In 5 patients with a normal cardiovascular system and 4 with hypertension, but without heart failure, tolazoline caused either a small rise or a fall in venous pressure and small and variable changes in arterial pressure and heart rate. In 3 cases of hypertensive or arteriosclerotic disease with congestive failure the drug caused a decrease in venous pressure of 12 to 80 mm. saline. The arterial pressure changes were small and the heart rate increased. In 6 cases of valvular heart disease with congestive failure the venous pressure fell by 5 to 28 mm. saline, the arterial pressure fell by 5 to 20 mm. Hg, and the heart rate increased. In 4 cases of chronic cor pulmonale with congestive failure the venous pressure fell greatly (25 to 146 mm. saline), the arterial pressure fell or remained the same, and the heart rate decreased or was unchanged.

Full digitalization with 1.5 mg. of digitoxin in one case of valvular heart disease and 2 of the cases of cor pulmonale decreased or abolished the action of tolazoline upon the venous pressure.

The authors conclude that tolazoline lowers venous pressure in congestive heart failure by releasing sympathetic venoconstriction. In cor pulmonale it is possible that the drug also antagonizes adrenaline-like metabolites produced by anoxic tissues.

L. G. Goodwin

1943. Treatment of Peripheral Vascular Disturbances with a New Vasodilator Substance "Dilatol". (Ein Beitrag zur Behandlung peripherer Durchblutungsstörungen unter Berücksichtigung einer neuen vasodilatatorischen Substanz Dilatol)

K. KAISER and H. MAURER. *Ärztliche Wochenschrift* [Ärztl. Wschr.] 6, 677-686, July 20, 1951. 3 figs., 12 refs.

This paper presents a critical comparison of the effects of 4 vasodilator drugs, tolazoline ("priscol"), "hydergin", "vasculat", and "dilatol" in a number of peripheral vascular disturbances. The 4 drugs were all tried on every patient so far as possible and the effect judged subjectively by the patient and objectively by estimation of the skin temperature in relation to the room temperature and by observation of the clinical picture. The effect of dilatol in increasing the minute-volume of the heart, in addition to its vasodilator action, is stressed. Absorption is rapid after oral administration

and the maximum effect is produced in 12 to 20 minutes. Toxicity is low in animals and tolerance to its side-effects, which consist in restlessness, tremor, and palpitations, develops so that the dosage may be increased.

The immediate effects of dilatol appear to be identical with those of tolazoline in arteriosclerotic conditions, and over a prolonged period its effect seems to be superior. No conclusions were reached on hydergin and vasculat owing to the small number of cases treated. Regarding the treatment of other diseases (Raynaud's disease, endarteritis obliterans, periarteritis nodosa) none of the preparations stands out as being particularly beneficial. The authors conclude that dilatol should be tried in vasomotor disturbances with an arteriosclerotic basis.

R. Hodgkinson

1944. An Emotional Faint

A. D. M. GREENFIELD. *Lancet* [Lancet] 1, 1302-1303, June 16, 1951. 2 figs., 4 refs.

An emotional faint with loss of consciousness lasting for 1½ to 2 minutes was induced in a susceptible medical student. The changes in the circulation shortly before, during, and after the faint were studied. The tachycardia present while the subject watched the preparations for the experiment gave way to marked slowing of the heart rate at the start of the faint, only 37 beats being recorded in the first minute. A Lead-II electrocardiogram was recorded continuously with an ink-writing instrument, but the record was not good enough for the analysis of the cardiac irregularities seen, especially during the recovery period. The forearm blood flow remained well above resting value (4 to 5 ml. as compared with 2 ml. per 100 ml. per minute) during the faint, while the blood pressure fell to 90/60 mm. Hg. These phenomena are taken as evidence of vasodilatation of the peripheral vessels in the forearm. The pallor of the skin would indicate that it is the vessels to the muscles which dilate in a way similar to that occurring in post-haemorrhagic fainting and mediated by sympathetic vasodilator fibres.

A. I. Suchett-Kaye

1945. Oral Hexamethonium Bromide in Essential Hypertension

W. A. MACKEY and G. B. SHAW. *British Medical Journal* [Brit. med. J.] 2, 259-265, Aug. 4, 1951. 2 figs., 8 refs.

The interim results of treatment of 15 cases of hypertension with oral hexamethonium bromide are presented. After preliminary investigations the patients were given test doses of the drug intramuscularly in doses of 25 mg. or more in order to detect any unusual sensitivity. The most convenient oral dosage was found to be 0.25 g. administered crushed, with water, before meals. The dose was gradually raised to 0.5 g. thrice daily before

meals for the average case, although in some cases 0.75 g. three times a day was necessary.

There was great improvement with initial disappearance of signs and symptoms in 5 cases; 10 were unimproved. Headaches were relieved in 7 cases. There was no reversal of retinopathy. The authors believe that this treatment is unaccompanied by any harm to the patient even if prolonged over a long period. The main disadvantages are: (1) that treatment is, of necessity, individualized and requires very careful adjustment; and (2) that a very small margin divides the effective dose from the disabling dose, so that it was found to be impossible in some cases to reduce blood pressure without producing disablement. *James W. Brown*

1946. The Effects of Intravenous Protoveratrine on Hemodynamics and Exercise Tolerance in Patients with Hypertension

F. W. LOVEJOY, P. N. G. YU, R. A. BRUCE, R. E. NYE, G. WELCH, B. B. BRODY, and J. MUXWORTHY. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* 222, 129-137, Aug., 1951. 4 figs., 8 refs.

A high blood pressure can be lowered and the heart rate slowed by giving veratrum viride, which acts by diminishing peripheral resistance through vasodilatation. The authors found considerable individual variation in the response of 19 hypertensive subjects to intravenous administration of protoveratrine, a crystalline derivative of *Veratrum album*. It was possible to obtain a relative bradycardia without significantly lowering the blood pressure or affecting the exercise tolerance, but with larger doses a more definite, yet temporary, hypotensive response resulted. Toxic nausea was uncommon. The drug produced electrocardiographic evidence of coronary insufficiency in 2 patients. Protoveratrine is not suitable as a therapeutic drug in hypertension.

J. L. Lovibond

ELECTROCARDIOGRAPHY

1947. Electrocardiographic Changes in Chronic Cor Pulmonale

J. A. KILPATRICK. *British Heart Journal [Brit. Heart J.]* 13, 309-318, July, 1951. 4 figs., 19 refs.

An analysis is made of electrocardiographic findings (bipolar and unipolar limb leads, and unipolar chest leads) in 20 cases of chronic cor pulmonale. The "P pulmonale", a sharply peaked P wave 2.5 mm. or more in height in standard leads or of 3 mm. or more in chest leads, was present in 60% of cases. Inversion of T in V₁, V₂, and V₃ was present in 85%. Right axis deviation was present in 85%, and in 30% it was marked, with depression of S-T and inversion of T₂ and T₃. In 25% of cases there was reversal of the R:S ratio in V₁, a deep S in V₆, delay of the intrinsic deflection to 0.03 to 0.05 second in V₁, and a tendency to a small Q in V₁, to inversion of T in V₁ and to an upright T in V₆, with QRS less than 0.12 second and absence of notching of R in V₁. Complete right bundle-branch block was not present in any case on admission, but developed 3

months later in 1 patient. Incomplete right bundle-branch block, defined as delay of the intrinsic deflection of V₁ or V_{3R} to 0.05 to 0.075 second, with a total QRS of 0.12 second or less, was noted in the right precordial leads in 20% of cases. There was a significant late R wave in aVR in all cases. In 25%, R in aVR was at least twice the size of S and there was a deep S in V₅. It is concluded that the late R in aVR (and in V_{3R}) is often related to right ventricular excitation in chronic cor pulmonale. Mean right intracardiac pressures were measured by saline manometry after cardiac catheterization in 12 cases, and no relation was found between either auricular or ventricular pressure and the presence of the "P pulmonale". Serial electrocardiograms were obtained in 13 cases, and 9 of these showed considerable improvement, including a diminution in the size of P and a decrease in the extent of T-inversion in the chest leads.

William A. R. Thomson

1948. The Variability of Ventricular Potentials at the Diaphragmatic Level of the Oesophagus

I. G. KROOP, M. F. STEINBERG, and A. GRISHMAN. *British Heart Journal [Brit. Heart J.]* 13, 369-380, July, 1951. 12 figs., 16 refs.

Synchronous electrocardiographic records were made in selected cases from within the oesophagus, inferior vena cava, or right atrium, and from the limbs or chest wall. The ventricular complex recorded from an oesophageal lead at diaphragmatic level was found to have a variable form; it appeared to be derived from the right ventricular cavity or surface potentials, or even the left ventricular cavity, rather than the left ventricular surface. The value of such an oesophageal lead in the diagnosis of posterior myocardial infarction is therefore questionable. A Q wave is often found which has no pathological significance, or which may really be an rS pattern derived from the right ventricular cavity, with the r too small to be seen without extra amplification.

The anterior relation of the oesophagus at the diaphragmatic level is shown not to be the left ventricle, but generally the inferior vena cava, or the right atrium when it is enlarged.

J. A. Cosh

1949. Correlation of the Electrocardiographic Pattern of Right Heart Strain and Evidence of Right Ventricular Hypertension in Congenital Heart Disease

A. GORDON and H. GOLDBERG. *American Heart Journal [Amer. Heart J.]* 42, 226-234, Aug., 1951. 2 figs., 14 refs.

The findings are presented of a study of 21 children under 15 years of age in whom there was either proven right ventricular hypertension (systolic pressure over 30 mm. Hg) or electrocardiographic evidence of right ventricular hypertrophy. The latter was diagnosed essentially on leads VR₄ and V₁, where the R wave was greater than S in children over 3 years of age, or where an R, but no S, wave was found after the first year of life.

All the 14 children aged between 3 and 15 years had right ventricular hypertension, which in 11 was accompanied by the electrocardiographic changes of right ventricular hypertrophy; in the remaining 3, complex

congenital anomalies may have caused an atypical electrocardiogram. The 7 children under 3 years had right ventricular hypertension, but the electrocardiogram was typical of hypertrophy in only one. Thus where the electrocardiogram showed right ventricular hypertrophy there was always right ventricular hypertension, but, especially in younger children, right ventricular hypertension could exist without typical electrocardiographic changes.

J. A. Cosh

1950. The Electrocardiogram in the First Two Months of Life

R. A. FURMAN and W. R. HALLORAN. *Journal of Pediatrics* [J. Pediat.] 39, 307-319, Sept., 1951. 2 figs., 17 refs.

1951. The Heart in Acute Hemorrhage: a Clinical and Electrocardiographic Study

S. DACK, E. CORDAY, and A. M. MASTER. *American Heart Journal* [Amer. Heart J.] 42, 161-183, Aug., 1951. 5 figs., 25 refs.

Electrocardiographic changes suggesting acute coronary insufficiency were observed in 25 of 28 patients suffering from haemorrhage. In 40% of these precordial pain or heart failure occurred. The authors consider that these changes are due to myocardial damage by ischaemia: sometimes the damage may amount to necrosis.

Changes in the electrocardiogram occurring between the sixth and sixteenth day after haemorrhage are described, but no conclusion as to their cause is reached.

D. Verel

HEART

1952. Pressure Curves from the Right Auricle and the Right Ventricle in Chronic Constrictive Pericarditis

A. T. HANSEN, P. ESKILDSEN, and H. GOTZSCHE. *Circulation* [Circulation] 3, 881-888, June, 1951. 8 figs., 13 refs.

Characteristic pressure curves were obtained by catheterization of the right auricle and right ventricle in 7 patients with constrictive pericarditis, and these reverted to normal in 2 patients after operation. The auricular pressure in this disease is always above normal and never reaches zero; mean pressure is relatively more elevated than maximal. In the ventricle the systolic pressure is slightly raised, but not outside the limits of normal, indicating an efficient systolic contraction. Having reached its minimum, the pressure again rises sharply to midway between minimum and maximum during diastole, where it forms a plateau preceding the systolic rise. This "diastolic dip" is characteristic; it is never seen in congestive failure or in pericardial effusion, and is due to the hampered diastolic dilatation which is a feature of this type of pericarditis. Besides being of value in diagnosis, such a curve may be a useful guide to operation in that a pronounced "diastolic dip" which almost reaches zero indicates a severe degree of constriction with an adequately functioning myocardium.

A. Paton

1953. Heart Puncture. II. Cardioangiography: Clinical and Electrocardiographic Results

V. B. NÚÑEZ and E. R. PONS DOMENECH. *American Heart Journal* [Amer. Heart J.] 41, 855-863, June, 1951. 11 figs., 3 refs.

In a previous paper (*Amer. Heart J.*, 1951, 41, 643) the authors described a method for direct intracardiac injection of diodone by heart puncture: 50 ml. of 75% diodone is injected under a pressure of 25 lb. per sq. in. (1.75 kg. per sq. cm.) into the right ventricle, and 30 lb. per sq. in. (2.11 kg. per sq. cm.) into the left. The authors report 45 punctures made on 30 subjects without fatality. In 30 instances the right ventricle was entered, in 15 the left. The results were unsatisfactory in only 2 cases. On recovering from the anaesthetic 18 patients had no symptoms, 8 had a transient slight "disturbance" in the upper abdomen or retrosternal region, and 4 noted some improvement in their condition. Pulse rate, blood pressure and electrocardiogram showed little abnormality during heart puncture. The most usual finding was the presence of ventricular extrasystoles as the trocar entered the heart wall, ceasing once the instrument had entered the chamber. Subsequently no abnormality was found on auscultation or x-ray examination. Three patients had fever the day after investigation. Of the 30 patients 5 died from carcinoma of the lung in from 7 days to 4 months after heart puncture. At 7 days small clots were present in the pericardial sac. After one month or more no evidence of heart puncture could be found.

D. Verel

1954. Low-salt Diet in Treatment of Congestive Heart Failure

A. L. NIELSEN, P. BECHGAARD, and H. O. BANG. *British Medical Journal* [Brit. med. J.] 1, 1349-1353, June 16, 1951. 17 refs.

The use of low-sodium diets in the treatment of cardiac oedema is reviewed. The authors then describe the results obtained in 64 patients with congestive heart failure with oedema who, in addition to receiving the usual treatment of rest in bed, digitalis, and diuretics, had a diet containing less than 1 g. of sodium chloride daily and were encouraged to take 2 to 3 litres of fluid. Marked improvement was seen in 36 patients who had failed to respond satisfactorily to routine treatment.

J. W. Litchfield

1955. The Liver in Heart Failure. Relation of Anatomical, Functional, and Circulatory Changes

S. SHERLOCK. *British Heart Journal* [Brit. Heart J.] 13, 273-293, July, 1951. 18 figs., 31 refs.

This study is based on the liver-biopsy or necropsy findings, or both, in 50 patients with congestive heart failure. Centrilobular hepatic necrosis was found in almost every case, the necrosis spreading peripherally as the failure worsened. Conversely, in cases responding to treatment the lesions might heal. Necropsy material was found to be unsatisfactory for assessing the effects of heart failure on the liver, because of the changes which occur in the agonal and immediate post-mortem periods. There was no correlation between right auricular

pressure and the extent of liver-cell necrosis. Cardiac cirrhosis was found in 13 cases, in 11 of which there was mitral stenosis. Although the cirrhotic lesion in heart failure may closely resemble Laennec's cirrhosis, no evidence of portal hypertension was found in this series. Serum bilirubin levels greater than 1 mg. per 100 ml. were found in 34 patients, and in 8 there was deep jaundice. The greater the degree of necrosis, the higher was the mean serum bilirubin level. Of the 8 patients with severe jaundice, 7 had mitral stenosis, and in 5 there was associated tricuspid incompetence. There was no correlation between cardiac output or arterial oxygen saturation and the depth of jaundice, but a correlation was established between the depth of jaundice and height of right auricular pressure. The mean serum bilirubin level was higher in patients with pulmonary infarction than in those without such infarction (3.2 mg. per 100 ml. as against 1.4 mg. per 100 ml. of serum). It is concluded that the exact cause of cardiac jaundice cannot be established and that cardiac cirrhosis has no specific clinical, blood-chemical, or circulatory association.

William A. R. Thomson

1956. Thromboembolic Phenomena Associated with Rapid Diuresis in the Treatment of Congestive Heart Failure

R. J. MARVEL and W. A. SHULLENBERGER. *American Heart Journal* [Amer. Heart J.] 42, 194-211, Aug., 1951. 12 figs., 31 refs.

In an attempt to assess the part played by haemoconcentration in the production of thrombosis the authors treated 12 patients with congestive heart failure with digitoxin, dietary sodium restriction, mercurial diuretics, "and so forth", and 3 others with congestive failure with a similar regimen without digitoxin. Two control subjects, free from oedema and from disease of the liver, heart, or kidney, were also given digitoxin, mercurial diuretics, and sodium restriction.

About a quarter of the patients with congestive heart failure developed thrombo-embolic complications between the 6th and 8th days of treatment, when haemoconcentration was maximal and such variable factors as increased prothrombin and fibrinogen values were present.

The series is too small to be statistically significant. The authors suggest that anticoagulant therapy may be desirable in selected cases.

D. Verel

1957. Aneurysms of the Sinuses of Valsalva

G. R. VENNING. *American Heart Journal* [Amer. Heart J.] 42, 57-69, July, 1951. 6 figs., 22 refs.

Seven cases of aneurysm of the sinus of Valsalva are reported. The lesion was thought to be congenital in one, probably congenital with superimposed endocarditis in 2, and the result of endocarditis in 4. In one case the rupture of the aneurysm into the right atrium was correctly diagnosed in life from the clinical and radiological findings. It was suggested by the sudden onset of failure in a patient who at the same time became aware of a noise in his chest. There was gross congestive failure, with marked venous pulsation, a collapsing pulse, a displaced, forceful apex beat, and a loud, rough,

continuous murmur greatest at the left sternal border by the 3rd and 4th spaces. There was electrocardiographic evidence of bundle-branch block with wide and bifid P waves. Radiological examination showed general cardiac enlargement and expansile pulsation in the small intrapulmonary vessels.

The embryology and the difficulty of interpreting the pathological findings in the presence of endocarditis are discussed.

D. Verel

1958. Aortic Aneurysm associated with Arachnodactyly
M. F. MOSES. *British Medical Journal* [Brit. med. J.] 2, 81-84, July 14, 1951. 4 figs., 19 refs.

The author briefly reviews the literature and notes that the number of necropsy reports on this condition is small, 26 in all. There were aortic lesions in one-half, but only 9 reports contained details of the histology of the aorta. This paper reports 2 further cases and includes post-mortem and histological findings. Both patients were women and had lesions of the lens in early life. Full details of the clinical and post-mortem findings and of the relevant histology are given. In one case there was dilatation of the aortic ring, a saccular aneurysm in the ascending aorta, and intimal tears in ascending and abdominal aorta, with no evidence of haematoma formation to the naked eye. Histologically, there were marked changes, chiefly fragmentation of the elastic fibres and gross oedema at the site of the tears, with a small haematoma into the adventitia at one place. There were also similar changes in one branch of the pulmonary artery. The second subject had a patent foramen ovale, dilated aortic ring, aneurysm of the ascending aorta, and 2 tears in the descending aorta. The histology at these sites showed mainly oedematous changes with some disappearance of the elastic fibres. The coronary arteries showed similar changes. The 13 previously reported cases all had similar lesions in the ascending aorta, and 7 had dissecting aneurysms; the 13 cases without aortic lesions all had heart lesions. The author points out that although a patent foramen ovale is assumed to be the most common cardiovascular lesion associated with arachnodactyly, aortic defects have been reported in 15 cases, whereas a patent foramen ovale occurred in only 8 cases. The lesions in the aorta are thought to be due to a congenital malformation of the media.

R. F. Jennison

1959. Calcification of the Aortic Valve and of the Coronary Arteries

D. PYKE and C. SYMONS. *British Heart Journal* [Brit. Heart J.] 13, 355-363, July, 1951. 8 figs., 22 refs.

Radiological examination of 400 men aged over 60, chosen at random, showed that 27 had calcification at some site in the heart. The coronary arteries were involved in 14, the aortic valve in 11, the mitral valve in 1, and the pericardium in 1.

Where the aortic valve was calcified there were physical signs suggesting aortic stenosis, such as an aortic systolic murmur, diminished second sound, and sometimes a thrill, but with a normal pulse pressure. In this group the patients were no younger than the

remainder of the 400; none had other evidence, or a history, of rheumatic heart disease, and a few were known to have developed a murmur late in life. The aetiology was therefore considered to be degenerative rather than rheumatic.

Where there was coronary arterial calcification, the circumflex branch of the left coronary artery was most often affected (9 out of 14). None of these patients had cardiac effort pain and only 1 had effort dyspnoea, he being 1 of the 4 patients with hypertension. Their ages were significantly greater than the remainder of the 400, again suggesting a degenerative aetiology.

On post-mortem radiological examination of 72 unselected hearts, calcification of the aortic valve was found in 22 (mainly at the line of attachment of the cusps) and calcification of the coronary artery in 38. It appeared that post-mortem radiography revealed calcification 8 times more frequently than naked-eye inspection.

J. A. Cosh

1960. The Use of Phenylephrine to Aid Auscultation of Early Rheumatic Diastolic Murmurs

E. M. M. BESTERMAN. *British Medical Journal* [Brit. med. J.] 2, 205-207, July 28, 1951.

The difficulty of recognizing mitral diastolic murmurs in the presence of tachycardia is well known. In order to prolong diastole, "phenylephrine" hydrochloride was given in doses of 0.25 mg. intravenously in children. This drug raises the arterial pressure in 2 minutes, and the pressure returns to normal in 4 to 8 minutes. The pulse rate falls by 36 beats per minute on the average, and the slowing lasts for 3 to 4 minutes. During this phase murmurs are intensified, vanished murmurs may reappear, and murmurs hitherto undetected may be brought out.

Of 64 patients, 1 complained of occipital headache and one of substernal oppression after the injection. The others had no symptoms. Accentuation of murmurs might outlast the effects on pulse and arterial pressure and might possibly be related to changes in stroke volume or other haemodynamic consequence of the drug.

J. McMichael

1961. Rheumatic Heart Disease in Patients over Sixty Years of Age

S. B. APPEL and C. E. KOSSMANN. *Journal of the American Medical Association* [J. Amer. med. Ass.] 146, 1474-1478, Aug. 18, 1951. 27 refs.

The case records of 71 patients over the age of 60 who had clinical signs of rheumatic carditis have been studied for an explanation of the patients' unusually long life. An initial attack of rheumatic fever at a late age (average 21.5 years) was the most consistent feature. There was no evidence that some other factors which have been suggested had influenced the length of life, such as the degree of mitral stenosis, ancestral longevity, and hypertension. It was found that 16 patients had had multiple attacks of rheumatic fever and 33 auricular fibrillation. As regards valvular lesions, 42 had mitral stenosis, 22 mitral and aortic disease, 3 mitral and tricuspid disease, and 4 aortic disease alone. Of the 20

patients who came to necropsy 5 had a "tight" mitral valve. The average duration of life after the first attack of congestive heart failure was 7.9 years, compared with 1.8 years in 138 patients with arteriosclerotic or hypertensive disease; cardiac disability of long standing may therefore indicate a rheumatic carditis.

Arthur Willcox

1962. Treatment of Incapacitated Euthyroid Cardiac Patients by Producing Hypothyroidism with Radioactive Iodine

H. L. BLUMGART, A. S. FREEDBERG, and G. S. KURLAND. *New England Journal of Medicine* [New Engl. J. Med.] 245, 83-91, July 19, 1951. 4 figs., 28 refs.

The authors, working in Boston, describe the treatment with radioactive iodine of 37 cardiac invalids who had normal thyroid function. The aim of the treatment is to reduce the metabolic rate so that the work of the heart is reduced. It is at best only palliative, but in one-third of the cases resulted in remarkable improvement, and in another third in worth-while improvement; in the remainder there was little benefit.

Cases both of angina and congestive cardiac failure were treated and the proportion relieved in the two groups was about equal. It may be 5 weeks to 6 months before the patient shows improvement after the treatment, so that it is not suitable for cases with rapidly progressive cardiovascular disease. Other contraindications are initially low basal metabolic rate and intermittent claudication. The aim is to reduce the basal metabolic rate to between -30% and -25%, and small doses of thyroid may be given if the patient becomes too myxoedematous. The authors do not believe that the high serum cholesterol level produced by the treatment increases the rate of progression of arteriosclerosis. They cite cases of heart disease in which thyroidectomy has been carried out and in which histological examination up to 11 years subsequently has failed to show any evidence of increased arteriosclerosis. It appears also that the "myxoedema heart" that occurs in these cases does not result in a worsening of the patient's condition, but usually coincides with an improvement.

G. S. Crockett

1963. Congenital Pulmonary Stenosis without Overriding Aorta. A Clinical Study

Y. LARSSON, E. MANNHEIMER, T. MÖLLER, H. LAGERLÖF, and L. A. WERKÖ. *American Heart Journal* [Amer. Heart J.] 42, 70-80, July, 1951. 8 figs., 15 refs.

Thirty patients aged 3 to 25 with isolated pulmonary stenosis were examined by cardiac catheterization, pressures being measured with the Hansen manometer. No patient was cyanosed, and most were without symptoms. The chief indication for investigation was a loud pulmonary systolic murmur. Stenosis was considered to be present when the right ventricular systolic pressure exceeded the systolic pressure in the main trunk of the pulmonary artery. Cardiac output and arterial oxygen saturation were normal. The difficulty of recognizing lesser degrees of stenosis at necropsy is thought to explain the rarity of the condition in necropsy records. The

authors regard pulmonary stenosis as probably fairly common, but suggest that only cases with marked ventricular hypertension need surgical treatment.

D. Verel

1964. Congenital Valvular Pulmonary Stenosis with or without an Interatrial Communication: Physiologic Studies as Diagnostic Aids

F. H. ADAMS, L. G. VEASY, J. JORGENSEN, A. DIEHL, J. W. LABREE, M. J. SHAPIRO, and P. F. DWAN. *Journal of Pediatrics* [J. *Pediat.*] **38**, 431-441, April, 1951. 1 fig., 7 refs.

1965. Congenital Absence of the Right Branch of the Bundle of His

J. B. COAKLEY. *British Heart Journal* [Brit. *Heart J.*] **13**, 148-152, April, 1951. 5 figs., 2 refs.

1966. Mitral Stenosis in Individuals of Advanced Age. (La estenosis mitral en personas de edad avanzada)

M. VELA, E. BENOT, and A. ZAMBRANO. *Revista Española de Cardiología* [Rev. esp. *Cardiol.*] **5**, 82-96, March-April, 1951. 7 figs., 5 refs.

Among 1,720 patients with pure mitral stenosis, 105 (6.1%) were 50 years of age and over. Of these, 92 were in the age group 50 to 59 years (69 females, 23 males), and 12 between 60 and 69 (10 females, 2 males). In 33 cases no aetiological factor was found in the history. Cardiac efficiency was normal in 5 patients, moderately impaired in 41, greatly impaired in 23, and cardiac failure was present at rest in 24. It is pointed out that mitral stenosis in advanced age is more frequent than is commonly assumed, although the present series shows a lower incidence than that of some other authors; this is attributed to the strict selection of cases in which a diagnosis of pure mitral stenosis without any other valvular lesion could be made with certainty on clinical and radiological grounds.

A. Schott

1967. Visibility of the Azygos Vein as a Radiological Sign in Tricuspid Lesions. (La visibilidad de la vena ázygos como signo radiológico de las lesiones tricúspideas)

A. AZPITARTE. *Revista Española de Cardiología* [Rev. esp. *Cardiol.*] **5**, 97-108, March-April, 1951. 7 figs.

On the basis of observations in 75 patients with tricuspid valvular lesions (13 with stenosis) it is pointed out that in all such cases the vena azygos is clearly visible in chest radiographs taken with the usual technique. It is claimed that this finding is so constant as to be of diagnostic importance. The shadow of the vena azygos is described as comma-shaped; its internal and superior part is thin and contiguous with the shadow of the wall of the right bronchus and trachea; its external and inferior part is blunt and thick. Sometimes the shadow is symmetrical and lancet-shaped. On an average it is 21 mm. long and 10 mm. wide. The visibility of this shadow in cases of tricuspid lesions is attributed partly to the distension of the vena azygos and partly to the outward displacement of the right bronchus by the enlarged left auricle.

A. Schott

1968. Relative Stenosis of the Tricuspid Valve. (Estenosis relativa de la tricúspide)

J. M. RIVERO CARVALLO, R. CARRAL, and M. H. RAMÍREZ JAIME. *Archivos del Instituto de Cardiología de México* [Arch. *Inst. cardiol. Méx.*] **21**, 47-60, 1951. 7 figs., 18 refs.

The case history, with radiographs, electrocardiograms, piezometric intracavitary tracings, and post-mortem findings, is given of a woman with essential pulmonary hypertension and pulmonary atherosclerosis in whom a relative stenosis of the tricuspid valve in the absence of valvular lesions was proved. This stenosis was due to marked right auricular and ventricular enlargement. The authors describe a diastolic rumbling murmur and a presystolic murmur, both caused by this relative stenosis in the same way as the Flint murmur is caused in the left heart. These murmurs are increased during deep respiration. Two further cases are mentioned in which, besides tricuspid organic valvular regurgitation without organic stenosis, there was a relative stenosis of the valvular ring giving rise to a diastolic tricuspid murmur.

René Mendez

ENDOCARDITIS

1969. Subacute Bacterial Endocarditis with Attacks of Haemolytic Jaundice Treated with Aureomycin. (Endocardite infectieuse évolutive avec poussées d'ictère hémolytique traitée par l'aureomycine)

H. METZGER and A. BLUM. *Strasbourg Médical* [Strasbourg *méd.*] **2**, 289-295, May, 1951. 14 refs.

The patient, a woman of 23 years, developed in 1946 an acute articular rheumatism with dyspnoea and palpitations accompanied by fever: similar acute attacks continued at intervals until early in 1950, when the patient developed an attack of acute haemolytic anaemia. She was then regarded as suffering from subacute bacterial endocarditis, although 6 blood cultures at different intervals were sterile, as were repeated bone-marrow cultures. Penicillin in doses of 15 mega units a day for 2½ months did not control the fever: nor did streptomycin, 1 g. daily for 2 months, or chloramphenicol, 30 g. in 14 days. When, however, aureomycin was given the temperature promptly fell. A total of 31.75 g. of aureomycin was given in 18 days and later, as a *cure de consolidation*, 2 g. daily for 15 days. The patient remained in good health for 5 months, but then had another attack of acute haemolytic anaemia which was again cured by aureomycin. Five weeks later she had a violent precordial pain and died very suddenly.

G. M. Findlay

1970. Bacterial Endocarditis. (Bakteriell endokarditt)

S. AARSETH and V. GAUSTAD. *Nordisk Medicin* [Nord. *Med.*] **46**, 1093-1098, July 18, 1951. 10 refs.

Fifty cases of bacterial endocarditis, of which 10 were acute and 40 subacute, were treated in Ullevål Hospital from May 1, 1945, to Sept. 1, 1950. Of the patients with acute disease 9 died, 8 shortly after admission and 1 of heart failure 4 months after treatment was stopped. Of

the patients with subacute disease 24 died, including 4 untreated and 11 while under treatment. Bacterial endocarditis was the cause of death, with contributory heart failure in 7 cases. Nine patients died after the treatment had been terminated, and the cause of death was relapse and heart or kidney failure in 3 cases, heart failure alone in 4 cases, and other diseases in 2 cases. Bacterial cure was obtained in 22 of the 36 cases treated. The deaths in patients with arteriosclerotic aortic valvular disease were especially numerous. Many of these patients belonged to the higher age groups. Of 21 patients over 40 years old, 17 died, and of 19 under 40 years, 7 died.

In half of the patients the diagnosis was made during the first 4 weeks of illness. Of those with subacute bacterial endocarditis 34 were treated with penicillin; 2 had at first a course of penicillin, but as the infection persisted streptomycin was given and resulted in lasting cure. Especially during the first period, too small doses of penicillin were administered, and all patients receiving a daily dose of less than 500,000 units died. Gradually both the daily and the total doses were increased considerably, with a notable improvement in the results. The largest daily dose was 16,000,000 units and the largest total dose approximately 650,000,000 units. The present routine treatment is 2,000,000 units a day for 4 to 6 weeks.

The type of infection was verified in 27 cases, while in 9 patients blood cultures were negative. In 4 cases the diagnosis was not made until necropsy. Streptococci belonging to the *viridans* group were found in 18 cases. In the others with positive blood cultures different micro-organisms were demonstrated. The best results of treatment were obtained in the *viridans* group. Auricular fibrillation occurred in 8 patients with subacute bacterial endocarditis, in 4 of whom it was paroxysmal; 4 patients probably had fibrillation before the onset of bacterial endocarditis.

The 17 patients still alive have been under observation for from 4 to 43 months, average 22 months. Only one of these is over 50 years of age. The average age at the time of treatment was 31½ years. A slight to moderate increase of the heart volume was demonstrated in 4 patients and in 2 the heart disease was slightly aggravated, but none had pronounced symptoms of insufficiency.

The diagnostic possibilities are discussed. The importance of early diagnosis is stressed, as well as early treatment with sufficient doses and determination of resistance to different antibacterial drugs.—[From the authors' summary.]

DISTURBANCES OF RHYTHM

1971. The Use of Procaine Amide in Cardiac Arrhythmias

H. J. KAYDEN, J. M. STEELE, L. C. MARK, and B. B. BRODIE. *Circulation* [Circulation] 4, 13-22, July, 1951. 5 figs., 3 refs.

Procaine given intravenously exerts an anti-arrhythmic action on the heart, but its stimulatory effect on the central nervous system limits its application. Procaine

amide, a synthetic analogue of procaine, retains the anti-arrhythmic activity, but has few toxic effects in therapeutic doses and is relatively stable in the body. It is rapidly and completely absorbed from the gastrointestinal tract, peak concentrations being obtained 1 to 2 hours after its oral administration. It is slowly excreted by the kidneys, the plasma level falling by about 15% per hour. About 60% is excreted unchanged in the urine. When renal function is normal, a plateau concentration can be reached in the plasma after 36 to 48 hours of repeated oral administration of a constant dose.

In 54 patients with premature ventricular contractions procaine amide, whether administered orally or intravenously, effectively suppressed the aberrant beats. In 13 of 15 patients with ventricular tachycardia the abnormal rhythm was terminated by use of procaine amide. Six of these patients had previously been treated with quinidine. Oral administration is preferable to intravenous unless the patient is comatose.

Administration of the drug should be controlled electrocardiographically. The maximum rate of injection should be 200 mg. per minute until aberrant rhythm has been suppressed or 1 g. given. When the drug is given orally, 1.25 g. may be given initially and, if the electrocardiogram shows no change in an hour, a second dose of 0.75 g. Further doses of 0.5 to 1 g. may be given every 2 hours until the aberrant rhythm is eliminated. Maintenance doses may be necessary, for which 0.5 to 1 g. should be given every 3 to 6 hours day and night.

F. A. Langley

1972. Procaine Amide: its Effect on Auricular Arrhythmias

A. I. SCHAFER, S. BLUMENFELD, E. R. PITMAN, and J. H. DIX. *American Heart Journal* [Amer. Heart J.] 42, 115-123, July, 1951. 3 figs., 4 refs.

Procaine amide has the quinidine-like action of procaine but is less rapidly inactivated. It restored sinus rhythm in one patient with paroxysmal auricular tachycardia due to digitalis, one patient with auricular flutter, and one with auricular extrasystoles. Of 11 cases of chronic auricular fibrillation, sinus rhythm was restored by oral therapy in 5. In 3 patients procaine amide appeared to induce ventricular extrasystoles. It did not restore sinus rhythm when given intravenously to 6 patients with auricular fibrillation.

The value of the drug is limited by its tendency to cause nausea and vomiting when given by mouth and hypotension and arrhythmia when given by injection.

D. Verel

1973. The Action of Procaine Amide in Cardiac Arrhythmias

H. MILLER, M. H. NATHANSON, and G. C. GRIFFITH. *Journal of the American Medical Association* [J. Amer. med. Ass.] 146, 1004-1007, July 14, 1951. 7 figs., 10 refs.

A dose of 500 mg. of procaine amide was administered by slow intravenous injection to 50 patients with cardiac arrhythmia. Ventricular premature systole was abolished within 1 minute in 26 out of 31 cases. The

effect lasted from 7 minutes to over 2 hours. Of 8 cases of ventricular tachycardia, normal rhythm was restored in 4 and the rate was slowed materially in another 4. Normal rhythm was also restored in 3 cases of supraventricular tachycardia, and the rate slowed in 1. Established fibrillation was unaffected, but a paroxysm of fibrillation ceased 1 minute after the injection. The drug is effective by mouth and can be given in doses varying from 0.5 g. three times daily to 1 g. 3-hourly either prophylactically or to terminate a paroxysm.

Reactions were mild and consisted in a bitter taste, flushing, or a moderate fall in blood pressure after intravenous injection, and gastric discomfort after oral administration. It would appear that this drug has a definite place in the control of the arrhythmias, especially those arising in the ventricle.

C. W. C. Bain

1974. The Treatment of Urgent Cases of Paroxysmal Auricular Fibrillation. A Proposed Method for Aiding in the Choice between Digitalis and Quinidine

E. HELLMAN, M. R. ALTCHECK, and C. D. ENSELBERG. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 655-660, June, 1951. 46 refs.

Digitalis was given intravenously to 27 patients with paroxysmal auricular fibrillation. In one case only was normal rhythm restored; slowing of the ventricular rate was achieved in one other case. Quinidine was given by mouth to 22 patients and normal rhythm was restored in 20. The smallest dose of quinidine required was 0.2 g.; the largest total dosage was 7.5 g., and the largest individual dose was 0.8 g.

The authors suggest that digitalis will not slow the ventricular rate unless heart failure is present. They consider, however, that it is worth giving intravenous digitalis first. If no slowing has occurred within an hour, quinidine by mouth should be substituted. [The use of intravenous quinidine is not mentioned.]

C. W. C. Bain

See also Pharmacology and Therapeutics, Abstract 1802.

CORONARY ARTERY DISEASE

1975. Effects of Dioxylone Phosphate and Enteric-coated Khellin on Coronary Artery Insufficiency

M. M. BEST and W. S. COE. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 222, 35-39, July, 1951. 13 refs.

The effects of dioxylone phosphate (6:7-dimethoxy-1:4'-ethoxyl-3-methoxybenzyl-3-methyl-isoquinoline), which is said to be "a synthetic compound similar to papaverine in chemical structure and physiological activity", and of enteric-coated tablets of khellin were investigated on 11 patients with clinical signs and symptoms of angina pectoris. The dose of the former was 1.2 g. daily, and of the latter 120 mg. daily. The results were assessed electrocardiographically by means of the exercise tolerance test, the anoxaemia test, and the

ergonovine test, and also symptomatically. Out of 32 tests carried out before treatment, the results of 31 (96.9%) were positive. After dioxylone phosphate, 11 of these reverted to normal, compared with 13 after khellin treatment. When a placebo was substituted the results remained positive. Precordial pain occurred in 24 tests before treatment, in 15 after dioxylone, and in 17 after khellin. Symptomatic relief occurred in 6 patients with dioxylone, in 7 with khellin, and in 1 during placebo therapy. Toxic symptoms, consisting of nausea, vomiting, and diarrhoea, occurred in 3 patients with dioxylone phosphate, and in 8 with khellin; they were more severe with khellin than with dioxylone phosphate.

[These results can hardly be described as impressive. The most that can be said is that the enteric-coating of tablets of khellin would seem to reduce the unfortunate side-effects of this drug to a certain extent, and that dioxylone phosphate has a slight beneficial effect on a few patients with angina pectoris. On general principles, a drug which produces nausea and/or vomiting is contraindicated in the treatment of angina pectoris, unless its pain-relieving action is much greater than that of glyceryl trinitrate.]

William A. R. Thomson

1976. Shoulder-Hand Syndrome following Myocardial Infarction. Treatment by Procaine Block of the Stellate Ganglion

D. M. SWAN and J. M. MCGOWAN. *Journal of the American Medical Association* [J. Amer. med. Ass.] 146, 774-777, June 30, 1951. 3 figs., 5 refs.

Reflex neurovascular dystrophy of the upper extremity may be due to many different causes. It has been reported as occurring in as many as 10 to 20% of cases of myocardial infarction. It is characterized by painful shoulder disability with stiffness, swelling, and pain in the fingers and hand. After 3 to 6 months there may be disappearance of shoulder pain and hand swelling, but stiffness and flexion deformity of the fingers increase and there may be atrophy of the hand muscles and subcutaneous tissues. Later, trophic changes in the hand are prominent, with contractures, osteoporosis, and subluxations. The technique of stellate-ganglion block is described in detail, and 3 cases are reported to illustrate the complete success of this form of treatment.

T. Semple

1977. Clinical Aspects of Coronary Heart Disease. An Analysis of 100 Cases in Patients 23 to 40 Years of Age with Myocardial Infarction

M. M. GERTLER, M. M. DRISKELL, E. F. BLAND, S. M. GARN, J. LERMAN, S. A. LEVINE, H. B. SPRAGUE, and P. D. WHITE. *Journal of the American Medical Association* [J. Amer. med. Ass.] 146, 1291-1295, Aug. 4, 1951. 18 refs.

The subjects of the authors' study of myocardial infarction were 97 men and 3 women in whom infarction developed before the age of 40. Of these patients 64 had preceding symptoms—angina, dyspnoea, or "indigestion". The attacks came on as a rule during the working day: in only 11 cases was the onset during sleep. In 21

instances the attack was related to some unusual activity, suggesting that effort might accelerate the process leading to infarction. The patients were of mesomorphic body build, shorter, more muscular, heavier, and broader than a control group, and they usually looked older than their chronological age. Blood cholesterol levels were higher on the average than in the controls of the same age. Attacks tended to come on during the winter months.

J. McMichael

1978. Digitalis in Acute Myocardial Infarction

J. M. ASKEY. *Journal of the American Medical Association* [J. Amer. med. Ass.] **146**, 1008-1010, July 14, 1951. 14 refs.

Digitoxin was given in 50 cases of myocardial infarction from the first week onwards in doses of 0.2 mg. three times daily for 2 days and then once daily, and the results were compared with those observed in 50 controls who received no digitalis. All patients with complications were excluded, as were those who had any form of arrhythmia when seen first. None of those receiving digitalis developed ventricular tachycardia; in fact, the results in the two groups were almost identical. It is argued from this that digitalis should be used more freely to combat early congestive failure in myocardial infarction.

C. W. C. Bain

1979. Prognosis of Angina Pectoris and Coronary Occlusion. Follow-up of 1,700 Cases

L. H. SIGLER. *Journal of the American Medical Association* [J. Amer. med. Ass.] **146**, 998-1004, July 14, 1951. 3 figs., 17 refs.

A statistical study was made of 1,700 patients with angina pectoris and coronary occlusion observed over a period of 25 years. Of these, 1,302 were males and 398 females. The ratio of males to females was thus about 3.2 : 1. Of the entire series, 1,021 were still living and 679 were dead. The onset of clinical manifestations was slow in 809 cases and abrupt, in the form of an acute coronary occlusion, in 891.

The over-all average age at onset for the entire series was 55.8 years. The youngest age was 20 years and the oldest 93 years. The average age at onset in the living group was 56.7 for females and 51.6 years for males; in the dead group, 57.8 and 54.7 respectively. The ages at onset in the order of frequency were between 50 and 59 years, 60 and 69 years, and 40 and 49 years. These comprised 87.9% of the males and 87.2% of the females. The balance were distributed in the ages younger than 40 years and older than 69 years, males comprising mainly the younger and females the older ages.

The average age at death for males was 58.8 years and for females 61.7 years. The youngest age was 23 years and the oldest 94 years. The percentage number of patients who lived beyond 60 years of age was 59.2% for women and 50.9% for men; beyond 70 years, 17.9% for females and 15.0% for males, and beyond 80 years, 3.7% for females and 2.3% for males.

The average length of survival of the 679 patients who died was 4.7 years for males and 4.5 years for females.

The shortest survival was 3 hours and the longest 35 years. The percentage of patients still living at the end of 5 years was 32.8 for males and 34.5 for females; at the end of 10 years, 10 for males and 9.4 for females; and at the end of 15 years 3.5 for males and 1.6 for females.

The average length of survival of the 1,021 patients that were still living was 5.3 years for males and 5.6 years for females. One patient was still alive 32 years after the onset of symptoms. The percentage of patients still living at the end of 5 years was 54.6 for males and 46.1 for females; at the end of 10 years, 15.1 for males and 15.4 for females, and, at the end of 15 years, 4.2 for males and 6.2 for females. Of 393 patients the cause of whose death was known, death was due to the underlying heart disease in 83.5% and to other causes in 16.5%.

Of 1,208 patients who had one or more attacks of coronary occlusion, 878 had the attack as a first manifestation of coronary disease. In 330 who had had symptoms previous to occlusion the average duration from the onset of symptoms to the first attack of coronary occlusion was 3.9 years for males and 3.4 years for females. The longest duration was 21 years and the shortest 2 hours.

In 785 patients who were still alive after one attack or more of coronary occlusion the average duration between the first attack and the time when records were reviewed was 4.9 years for males and 4.5 years for females. About 45.3% of the males and 37.8% of the females were alive 5 years or more; 10.7% and 10.4% respectively, 10 years or more, and 2.1%, 15 years or more.

In 423 patients with coronary occlusion who ultimately died the average longevity after the first attack was 3.8 years for males and 3.1 years for females. About 68.4% of the males and 84.8% of the females died within 4 years after the first attack; about 31.6% of the males and 15.2% of the females lived 5 years or longer; 8.8% of the males and 7.2% of the females 10 years or longer, and 1.5% of the males and 1.6% of the females 15 years or longer.

This study, like every other study of this kind, is based on the duration of the clinical manifestations of degenerative coronary disease, not on the duration of the evolution of the structural pathology from its inception. The early phases of the latter, lasting many months or years, are undoubtedly asymptomatic in most cases and, therefore, antecede the clinical manifestations by that length of time. The entire duration of the evolution of structural coronary disease can, therefore, not be ascertained.—[Author's summary.]

1980. Prognosis and Treatment of Cardiac Infarction. A Survey of 200 Patients

C. PAPP and K. S. SMITH. *British Medical Journal* [Brit. med. J.] **1**, 1471-1478, June 30, 1951. 30 refs.

The authors classified 200 consecutive cases of cardiac infarction, drawn from consultant, general, and private practice, according to the severity of the disease. The prognosis for the patients in each group was investigated, and an attempt made to define the type of case suitable for anticoagulant therapy. The ages of the patients ranged from 34 to 75 years, the sex ratio was 5 men to

1 woman, and the over-all mortality was 25%, being about equal in the sexes. For "slight" cardiac infarction, in which shock and cardiac failure were absent, and "moderate" infarction, where these complications appeared only for a short time, mortality was less than 2% during the first 2 months of observation. The incidence of thrombo-embolic complications was negligible. The authors therefore suggest that these patients need not be treated with anticoagulants.

The mortality for the group with persistent circulatory shock and early congestive failure, implying a "severe" cardiac infarction, was 50% when anticoagulants were not used, two-thirds of the deaths occurring within the first 2 months. The value of anticoagulants was confirmed in a smaller series of cases of this type. The incidence of real embolic complications was 15%. The success of anticoagulant therapy was attributed to reduction of the thrombogenic effect of circulatory shock on the myocardium, lungs, and peripheral circulation rather than to the prevention of embolism.

Walter Somerville

BLOOD VESSELS

1981. Three Cases of Haemangioma with Osteohypertrophy (Klippel-Trenaunay). (Trois cas de nævus variqueux ostéo-hypertrophique de Klippel-Trenaunay) L. C. A. VAN DER HARST. *Annales de Dermatologie et de Syphiligraphie* [Ann. Derm. Syph., Paris] 78, 315-320, May-June, 1951. 4 figs., 12 refs.

The author describes 3 cases of haemangioma with osteohypertrophy. In 1 patient there was a distinct difference in blood pressure between the affected and the unaffected limb, suggesting an arterio-venous communication. These affections might be classified among the phacomatoses.

James Marshall

1982. Hypertensive and Nonhypertensive Periarteritis Nodosa

S. L. WILENS and J. GLYNN. *Archives of Internal Medicine* [Arch. intern. Med.] 88, 51-60, July, 1951. 36 refs.

In a study of 28 cases from Bellevue Hospital, New York, and 66 from the literature, an attempt is made to determine the importance of hypertension in the development of periarteritis nodosa and to establish its relationship to hypersensitivity, also a common feature in the disease. Hypertension precedes the development of lesions in a percentage of cases which may be between 10 and 50 and which, the author contends, may well be nearer the latter figure in that some cases in which hypertension is discovered simultaneously with the disease show several points of resemblance to those where hypertension is pre-established. Observations thought to support the predisposing influence of hypertension are these: the lesions are most commonly found, and are most numerous, in organs of the splanchnic area, the area in which the necrotizing arteriolar lesions of hypertension are commonest; some cases of necrotizing arteriolitis are difficult to distinguish from periarteritis

nodosa; pulmonary arteriolitis has been noted in pulmonary hypertension from mitral stenosis, and lesions of periarteritis nodosa have been found in the lung in pulmonary hypertension from cardiac malformation; rats with renal disease and cardiac hypertrophy (and, presumably, hypertension) and animals with experimental renal hypertension frequently show similar periarteritic lesions; and analysis of this series tends to indicate that periarteritis nodosa is more liable to develop in non-allergic individuals with hypertension than in non-allergic individuals with no hypertension.

The increased arterial pressure is thought to favour the entry of the reactive substance into the arterial wall; in the predominantly hypertensive cases this penetration would probably not occur in the absence of heightened pressure; in the non-hypertensive cases, a higher proportion of which show hypersensitivity, entry can apparently be effected under normal arterial pressure. Some objections to the theory (absence of lesions from large elastic arteries and from the left ventricular endocardium; periarteritis nodosa limited to the pulmonary artery) are considered.

In the non-hypertensive group the arterial lesions were more widespread in the organs and more profuse than in the group with antecedent hypertension, and involved the larger as well as the smaller arteries.

R. Crawford

1983. Peripheral Circulatory Changes Associated with Arteriovenous Aneurysms

G. M. WILSON. *British Heart Journal* [Brit. Heart J.] 13, 334-342, July, 1951. 4 figs., 22 refs.

In this investigation 2 cases were studied—one with an aneurysm between the deep femoral vessels, and the other with an aneurysm in the vessels of the thenar eminence. In the first case the peripheral blood flow was estimated by enclosing the foot in a venous-occlusion plethysmograph. Although the blood pressure in the leg below the fistula was lower than on the normal side, the blood flow through the foot was slightly greater. Digital closure of the fistula caused a rise in brachial blood pressure and a slowing of the pulse. The electrocardiogram showed abnormal P waves and a long P-R interval, probably the result of vagal activity.

In the second case the blood flow through the fingers was estimated by measuring the heat-elimination with a calorimeter. The flow on the affected side was much lower than on the normal; digital closure of the fistula increased the blood flow to above normal. Compression of the artery above the aneurysm decreased the blood flow in the fingers.

These observations showed that although the pressure in the arteries distal to the fistula was low, the vessels had enlarged, perhaps under the stimulus of metabolites formed in the ischaemic tissue. Extirpation of the fistula is the only satisfactory treatment; interference with the proximal artery may seriously endanger the blood supply to distal tissues.

L. G. Goodwin

See also Pathology, Abstract 1863; Medicine: General, Abstract 1941.

Disorders of the Blood

1984. The Central Nervous System Manifestations of Besnier-Boeck-Schaumann Disease. (Die zentralnervösen Erscheinungsformen des Morbus Besnier-Boeck-Schaumann)

A. F. ESSELLIER, B. J. KOSZEWSKI, F. LÜTHY, and H. U. ZOLLINGER. *Schweizerische Medizinische Wochenschrift* [Schweiz. med. Wschr.] **81**, 376-382, April 21, 1951. Bibliography.

This report is based on the literature and on the authors' personal experience. The affection appears to be characterized by extreme variability of the neurological symptoms and by its progressive development with exacerbations and remissions. Three forms may be distinguished: (1) the purely meningeal type (rare); (2) the purely encephalitic type (also rare); and (3) the usual form of chronic meningoencephalitis. Any part of the central nervous system may be involved, including the hypophysis. Of the cranial nerves, the facial appears the most vulnerable. Diabetes insipidus is not a rare complication; but the disease may be confined, for example, to the cord. The diagnosis is based on the presence of other manifestations of the disease, such as in the skin or lungs, and the absence of other aetiological factors, such as parotitis, scarlet fever, or measles; but in default of other indications the diagnosis is rendered highly probable by the characteristic form of development of the disease and the capricious manifestations of the neurological symptoms, often varying from day to day.

S. Burgi (Excerpta Medica)

ANAEMIA

1985. Familial Leptocytosis (Cooley's Anemia and Cooley's Trait). Observations on Three Families, with a Related Study of Bone Marrow Activity

H. E. HAMILTON and W. M. FOWLER. *Archives of Internal Medicine* [Arch. intern. Med.] **87**, 825-834, June, 1951. 1 fig., 30 refs.

Three families, 2 of Greek and 1 of Italian origin, are described to illustrate the main features of Cooley's trait and Cooley's anaemia. In 2 of the families there were several individuals who showed the typical haematological picture of Cooley's trait (normal or polycythaemic erythrocyte counts, low mean corpuscular haemoglobin, low mean corpuscular volume, and increased resistance to haemolysis in hypotonic solutions). The affected persons appeared to be otherwise healthy and led normal and active lives. In the third family there were 2 children, both suffering from Cooley's anaemia and requiring periodic transfusions every 6 to 8 weeks. Both the parents showed the characteristic features of Cooley's trait. These findings were consistent with the currently accepted view that individuals with Cooley's trait are heterozygous for a gene which, in homozygous form, leads to the development of the severe anaemia.

Detailed haematological studies on the 2 anaemic children are given. Marrow specimens obtained in each case on two occasions approximately one year apart were indistinguishable. Differential counts of the marrow revealed a great preponderance of early erythroblasts. There occurred also an apparent inability of the developing erythrocytes to acquire haemoglobin, so that although the nuclear elements appeared to develop normally throughout the entire maturation process, the cytoplasm failed to show even a minimal complement of haemoglobin until the late erythroblastic or early normoblastic stage. The myeloid elements were decreased in total numbers, but the distribution of the cell types was normal.

Periodic erythrocyte and reticulocyte counts were made over a period of 4 years in one case and 2 years in the other. With a falling erythrocyte count the release of reticulocytes was minimal or absent, whereas when the total cell count was increasing or remained constant there was an associated reticulocytosis. This implied a periodic depression and acceleration of erythropoiesis. Iron-balance studies in one infant revealed no abnormality.

Harry Harris

1986. The Heavy-metal Content of Liver Extracts. (Sul contenuto in metalli pesanti degli estratti epatici)

B. PERNIS, P. CAMERADA, M. CONGIU, and P. LEO. *Haematologica* [Haematologica] **35**, 429-435, 1951. 13 refs.

The amount of cobalt, nickel, copper, and zinc in 4 liver extracts was estimated polarimetrically. Clinical and haematological activity was related to the cobalt content and to a lesser extent to the content of nickel and zinc. The less active extracts had a higher copper content.

E. Neumark

1987. Haemosiderin Phagocytosis in the Plasma Cells of the Bone Marrow. (Über die Hämosiderinphagozytose in den Knochenmarksplasmazellen)

B. J. KOSZEWSKI. *Helvetica Medica Acta* [Helv. med. Acta] **18**, 175-191, June, 1951. 6 figs., bibliography.

This "contribution to the physiopathology of the bone marrow" is based on the careful study of 3 patients with pernicious anaemia and haemosiderosis, 2 of whom came to necropsy. As controls 9 cases of haemochromatosis, 30 of cirrhosis of the liver, and 37 of megalocytic anaemia were studied, but phagocytosis of haemosiderin by bone-marrow plasma cells was not seen in any of these. The proportion of plasma cells in the bone-marrow of the patients was 4.2 to 18%, 1.2 to 3% containing numerous inclusion bodies of dark-brown-staining pigment. All the marrow specimens were megaloblastic. In the 2 necropsies recorded haemosiderosis affected liver, pancreas, spleen, and lymph nodes. [It is not stated whether inclusion bodies were also seen in post-mortem

histological preparations.] In the patient still surviving, the first observation of pigmentary inclusion bodies in plasma cells coincided with the transformation of macrocytic anaemia with a large cell size to megalocytic anaemia with high mean cell volume.

The conclusion drawn from this study is that plasma cells should not be regarded as a distinct series of cells, but as part of the reticulo-endothelial system of the bone marrow.

E. Neumark

1988. Juvenile Pernicious Anemia

E. H. REISNER, J. A. WOLFF, R. J. MCKAY, and E. F. DOYLE. *Pediatrics* [Pediatrics] 8, 88-106, July, 1951. 6 figs., 43 refs.

The authors have reviewed the incidence of pernicious anaemia or pernicious-like anaemia in children as gathered from the literature since 1927, and found that only 12 cases could be accepted as instances of true pernicious anaemia in children. Their criteria for diagnosis were macrocytic anaemia with megaloblastic bone marrow in the absence of other causes of megaloblastic haematopoiesis, and the need for continued specific therapy to prevent relapse. They do not hold the view that the presence of free hydrochloric acid excludes the diagnosis of true Addisonian pernicious anaemia.

They present the histories and describe the investigations in 4 further cases occurring in 2 pairs of sibling children aged from 3½ to 9½ years which presented all the features and all the symptoms of adult pernicious anaemia with the exception of persistent histamine-refractory achlorhydria and premature greying of the hair. The haematological findings were identical with those of adult pernicious anaemia and all the patients responded to vitamin B₁₂ given parenterally. Neurological symptoms appeared in 3 of them, being severe in 2. In one of these patients treatment with folic acid aggravated the neurological lesions.

R. Winston Evans

1989. Elliptocytosis in Erythrocytes as a Morbid Sign. (Die Elliptocytose der roten Blutkörperchen als Krankheitszeichen)

F. ZINI and H. LEUBNER. *Schweizerische Medizinische Wochenschrift* [Schweiz. med. Wschr.] 81, 382-384, April 22, 1951. 21 refs.

Elliptic erythrocytes may be seen not only in constitutional elliptocytosis, but also in various other diseases as symptomatic elliptocytosis. The presence of poikilocytes at the same time is more characteristic of the symptomatic form (in pernicious anaemia, haemolytic jaundice, acute anaemia due to haemorrhage, chronic myeloid leukaemia, chronic lymphadenosis, pulmonary tuberculosis, and endocarditis lenta). The degree of symptomatic elliptocytosis runs parallel to the severity of the anaemia. Elliptocytosis is particularly pronounced in pernicious anaemia and does not completely disappear with liver therapy. Particulars of the technique for accurate diagnosis and classification of the elliptic erythrocytes into 5 groups are given.

U. Haenel (*Excerpta Medica*)

1990. Sick Cell Disease: Studies on *in vivo* Sickling and the Effect of Certain Pharmacological Agents

A. B. HENDERSON. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 628-635, June, 1951. 4 figs., 17 refs.

The object of this investigation was to observe the degree of sickling *in vivo*, intravascular haemolysis, and anaemia during the chronic and acute phases of sickle-cell disease to seek a clue to the causes of the onset of the acute phase. Eight patients were studied for prolonged periods, including both acute and quiescent phases; 8 were studied only in the quiescent phase and 10 only during acute crises.

The results were surprisingly negative. No evidence of sudden massive destruction of erythrocytes before or during the crisis was found; instead there was a steady increase in intravascular haemolysis. Variations in the severity of sickling *in vivo* were not correlated with the onset of acute phases; sometimes very severe sickling occurred during the quiescent phase without any clinical symptoms, and there was no evidence of increase during the acute phase. The effects of the following measures on the three phenomena mentioned were also studied: blood transfusion; an anticoagulant—dicoumarol; an oxidation-reduction agent—methylene blue; an agent to increase blood flow—tetraethylammonium chloride; and a high-calorie diet. Nothing of consequence was learned from this study. The author suggests that changes in the rate of blood flow to organs are more important than any changes in the blood itself.

M. C. G. Israëls

See also Genetics, Abstract 1761.

HAEMORRHAGIC DISEASES

1991. Demonstration of a Thrombocytopenic Factor in the Blood of Patients with Thrombocytopenic Purpura

W. J. HARRINGTON, V. MINNICH, J. W. HOLLINGSWORTH, and C. V. MOORE. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 38, 1-10, July, 1951. 6 figs., 14 refs.

The aetiology of idiopathic thrombocytopenic purpura has been thought to depend upon either a depressed megakaryocyte activity or an increased platelet lysis. The present investigation suggests a further possible cause of the condition—the presence of a thrombocytopenic factor in the blood of such patients. The blood from 8 to 10 patients with this condition produced a profound reduction in the number of circulating platelets when transfused in volumes of 250 to 500 ml. into normal volunteers. The decrease was of the order of 50% of the initial count, was maximal 2 to 3 hours after injection, was maintained for 5 to 7 days, and was often accompanied by haemorrhagic symptoms similar to those of thrombocytopenic purpura. Transfusions from control subjects had no such effect.

In patients who underwent splenectomy the thrombocytopenic factor was persistent, even though the platelet count had improved. Initial studies suggest that the

active factor is contained in the globulin fraction of plasma—a fact of interest in view of the finding of Evans *et al.* (*Arch. intern. Med.*, 1951, **87**, 48) of platelet agglutinins in the plasma of patients with idiopathic thrombocytopenic purpura or that caused by sedormid sensitivity.

H. Payling Wright

1992. The Occurrence of Haemophilia in the Human Female

C. MERSKEY. *Quarterly Journal of Medicine [Quart. J. Med.]* **20**, 299–312, July, 1951. 8 figs., 37 refs.

The author begins by pointing out that to establish the diagnosis of haemophilia in the female it must be shown that: (1) both her parents could have transmitted the disease; (2) all her sons are haemophilic and the daughters either affected or carriers; and (3) the disease is clinically and pathologically indistinguishable from that which occurs in the male. Cases in which a haemophilic man marries a heterozygous female carrier usually involve the marriage of cousins. Very few examples of such marriages have occurred in known haemophilic families, but the author has been able to re-examine 2 of the affected females and some of the males of a family in which such a first-cousin marriage had occurred. The family was first reported by Treves in 1886, included by Bulloch and Fildes in their 1911 survey, and reported in 1935 in much detail by Handley and Nussbrecher: Treves thought that the little girl he had to deal with had haemophilia; the later examiners thought that the disease was not true haemophilia because in the first 3 generations known there was evidence of transmission from father to son. Such a mode of transmission is unknown in true haemophilic families. In the 4th generation an affected male married his first cousin, whose mother had 3 haemophilic brothers; this cousin marriage produced 12 children, and 2 males and 4, possibly 5, females suffered from a haemorrhagic disease. In the 5th generation 2 of the affected females had sons who were affected, and the possibly affected female had 4 affected sons.

The author has been able to re-examine 2 of the affected females in the 5th generation. One was 67 years old; she had a history of repeated excessive bleeding from trauma and dental extractions; she had had haematuria, a haematemesi, and several episodes of haemarthrosis; she had had severe menorrhagia, but had successfully borne 3 children—2 apparently normal daughters and a son who was clinically affected and had haemarthroses. On examination she was seen to have several bruises, and some joints showed typical radiological changes like those seen in haemophilia. The clotting time (Lee and White) of her blood was at the upper limit of normal, but the clotting time of recalcified plasma, the prothrombin consumption test, and the test for ability to correct the clotting defect of known haemophilic plasma, all gave results like those of true haemophilia. The laboratory examination of the blood of her affected son showed results just outside normal limits; this was clinically a definite case of haemophilia.

The second sister was 57 years old; she had bled excessively from cuts and after dental extractions; she had had haematuria, menorrhagia, and mild episodes of

haemarthrosis that had produced no radiological changes. Her clotting time (Lee and White) was 12½ to 13 minutes compared with a normal maximum of 10 minutes, and the prothrombin consumption index was 44%, compared with the normal maximum of 40% and the 100% of her sister; the results of the test of the effect on known haemophilic plasma clearly indicated a diagnosis of haemophilia. This patient had one affected son; his blood was not examined.

Another sister (age not recorded) had similar symptoms; she had a mildly prolonged clotting time and the prothrombin consumption test was within the upper normal limit; no test on known haemophilic plasma was done. She is recorded as “probably affected” and she had 4 affected sons. Two of these sons were examined by the author and were found to have typical haemophilia with clotting times at the upper limit of normal.

The author emphasizes that in patients like these, in whom the usual tests give results within the upper limit of normal, the deciding factor is the effect of their plasma on the plasma of known haemophilic subjects. By this criterion the 2 sisters he tested had haemophilia. The only laboratory finding against the diagnosis of haemophilia was that the sister aged 67 had a positive tourniquet test, and that faintly positive reactions were obtained in the sister aged 57 and in one of the 6th-generation males. The author points out that the history of bleeding in the males of the first 3 generations is scanty and no more than traditional. The mode of inheritance and the laboratory findings from the 5th generation onward would fit haemophilia, and the author considers that, in spite of the absence of satisfactory evidence about the 4th-generation parents, the family now exhibits true haemophilia of the type without grossly prolonged clotting time of the blood and that the 2 females examined had the disease.

M. C. G. Israëls

LEUKAEMIA

1993. The Effect of Oestrogens and of Testosterone on Haematopoiesis in Leukaemia. (L'azione degli estrogeni e del testosterone sull'emopoiesi dei leucemici) E. STORTI, C. MAURI, and N. MOCCHI. *Haematologica [Haematologica]* **35**, 493–555, 1951. 10 figs., bibliography.

After reviewing the literature dealing with the relationship of leukaemia and sex hormones the authors report on 17 patients who were treated with testosterone propionate or with stilboestrol and allied preparations, usually in courses lasting 2 to 3 months, but sometimes longer. In this series there were 3 patients with acute myeloid leukaemia, 2 with acute lymphatic leukaemia, 6 with chronic myeloid leukaemia, 5 with chronic lymphatic leukaemia, and one with Hodgkin's disease. The development and ultimate result of the diseases were not altered by the treatment, though in a few patients clinical changes mainly involving a reduction in the size of spleen or lymph nodes, and sometimes a moderate fall in leucocyte count and temporary improvement in the bone-marrow picture, were recorded.

E. Neumark

1994. **Behaviour of Eosinophils and Neutrophils in the Bone Marrow in Leukaemia.** (Ricerche comparative sul comportamento degli eosinofili e dei neutrofili nel midollo osseo nelle leucemie)

C. SACCHETTI and M. F. SACCHETTI-LEATI. *Haematologica* [*Haematologica*] **35**, 339-373, 1951. 7 figs., bibliography.

The bone marrow was studied in 5 healthy individuals and 5 patients with chronic myeloid leukaemia, 5 with chronic lymphatic leukaemia, 2 with chronic eosinophilic leukaemia, 5 with stem-cell leukaemia, 5 with acute myeloid leukaemia, 5 with Hodgkin's disease, 4 with *Ankylostoma* infestation, and 1 suffering from threadworms.

Myelograms were recorded and maturation curves of neutrophils and eosinophils plotted. The average proportion of eosinophils in normal bone marrow is 6.3%, and maturation curves show a higher peak for eosinophils than for neutrophils, but for both types the maximum is at the myelocyte stage. In chronic myeloid leukaemia, though the number of eosinophils was only 2 per 100 marrow cells, their behaviour as regards maturation followed the pattern of the neutrophil cells. In chronic lymphatic leukaemia neither neutrophil nor eosinophil cells were abnormal. In chronic eosinophilic leukaemia there were about 60% eosinophil cells showing similar changes to those in chronic myeloid leukaemia, but the eosinophils were not affected in acute myeloid leukaemia. In Hodgkin's disease maturation of eosinophils was not affected, and in only 1 of 5 cases was there a significant increase in number of eosinophils, to 16 per 100 marrow cells. In the patients with parasitic infestation eosinophils numbered 6.6 to 18.6 per 100 marrow cells, but their maturation was normal.

E. Neumark

1995. **Pituitary Adrenocorticotrophic Hormone (ACTH) and 11-Dehydro-17-hydroxycorticosterone (Cortisone) Therapy in the Leukemias and Lymphomas of Children**

C. E. SNELLING, W. L. DONOHUE, B. LASKI, and S. H. JACKSON. *Pediatrics* [*Pediatrics*] **8**, 22-33, July, 1951. 4 figs., 20 refs.

The authors report the results obtained in the treatment of 16 cases of leukaemia and 1 case of lymphosarcoma with either cortisone or ACTH. The primary treatment in 13 of the cases was with ACTH, and cortisone was used initially in 4 of the cases. When relapses occurred, further treatment was given with either the original hormone or the alternative. In a few patients who became refractory to further treatment aminopterin was administered.

Of 8 patients who received ACTH before any other form of treatment had been given 6 had remissions which lasted from 3 to 13 weeks; the other 2 patients showed only negligible response despite large doses of ACTH. Five patients received aminopterin before ACTH therapy; of these one patient had a complete remission which lasted 10 weeks. Only negligible responses were obtained in the other 4 cases.

Retreatment with ACTH of 5 children whose condition had relapsed elicited a favourable response, lasting 6 weeks, in only one instance. The total amount of

ACTH given ranged from 680 to 2,300 mg. and the dose varied from 20 to 200 mg. per day.

Four patients received cortisone as the primary therapeutic agent. Of these, 3 suffered from leukaemia and one from lymphosarcoma. One leukaemic patient had a complete remission, while the others showed no response. The remission lasted for 4 weeks only and was followed by a relapse, which was refractory to treatment with both ACTH and aminopterin. A temporary response with shrinkage of the tumour mass in a case of lymphosarcoma was obtained, but this lasted only 2 weeks.

Details of biochemical observations are given, and these seem to suggest that when a remission was produced this coincided with a mass destruction of leukaemic tissue.

R. Winston Evans

1996. **Effects of ACTH and Cortisone on Leukemia in Childhood**

I. SCHULMAN, J. T. LANMAN, O. E. LAXDAL, and L. E. HOLT. *Pediatrics* [*Pediatrics*] **8**, 34-52, July, 1951. 7 figs., 23 refs.

In the study reported 14 children suffering from leukaemia were treated with either ACTH or cortisone. Each substance was used as the initial therapy in 7 cases, though various changes and combinations were introduced later on.

In 6 children with acute leukaemia complete clinical and haematological remissions were obtained, but in 2 other children with acute leukaemia partial remissions only occurred. No response was obtained in 6 cases in children, including one case of acute leukaemia, cases of monocytic leukaemia, subacute and chronic myeloid leukaemia, and one case of lymphocytic leukaemia. Four children in this refractory group had received previous antileukaemic therapy.

The clinical remissions lasted from 1 to 33 weeks and the improvement was often rapid and dramatic in onset.

R. Winston Evans

1997. **Considerations on Sarcolemucosis (Leukemia of Lymphosarcomatous Cells).** [In English]

G. PANIAGUA, M. MORALES PLEGUEZUELO, and C. JIMÉNEZ DJAZ. *Bulletin of the Institute for Medical Research* [*Bull. Inst. med. Res., Madr.*] **4**, 15-64, Jan.-March, 1951. 39 figs., 31 refs.

The authors describe 12 patients in whom the clinical and haematological features of acute lymphatic leukaemia were associated with local lymphoid masses having the infiltrative quality of lymphosarcoma. There was usually generalized enlargement of lymph nodes with lymphoid infiltration of other tissues (thymus gland, liver, kidney). At some stage malignant "sarcolemucocytes" were found in blood and bone marrow in every case, and this type of cell was thought to be diagnostic of the condition. Of the 12 patients 11 were males and 10 were children or young adults. Temporary remissions were observed once after urethane treatment and twice after radiotherapy, but deterioration was usually rapid. A Pel-Ebstein type of fever occurred in several cases. This group of patients formed more than 50% of all cases of acute lymphatic leukaemia seen since 1940.

P. C. Reynell

Respiratory Disorders

1998. The Significance of Fat in Sputum

W. F. NUESSELE. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] **21**, 430-435, May, 1951. 35 refs.

1999. Carbon-dioxide Intoxication in Emphysema: Emergency Treatment by Artificial Pneumoperitoneum

J. J. CALLAWAY and V. A. MCKUSICK. *New England Journal of Medicine* [New Engl. J. Med.] **245**, 9-13, July 5, 1951. 1 fig., 38 refs.

In this report it is contended that the administration of oxygen to patients with chronic anoxaemia results in an elevation of the carbon dioxide content of the blood due to removal of the anoxaemic stimulus to respiration. It is particularly marked in cases of severe emphysema, and results in a characteristic syndrome consisting of headaches, cutaneous vasodilatation, confusion, and stupor. The headaches are thought to be due to dilatation of the cerebral vessels, but the confusion and coma to a direct action of the increased carbon dioxide tension. In patients whose anoxaemia is caused by congestive heart failure the syndrome is often reversible, since pulmonary ventilation improves with treatment. But in severe emphysema the poor ventilation cannot be corrected by the usual treatment and recovery from the comatose stage is rare.

Artificial pneumoperitoneum, which was first introduced by Reich in 1924 for the treatment of emphysema, appears to improve pulmonary ventilation by raising the diaphragm and reducing the amount of residual air. Only one case treated by this method is described. The patient, a man of 56 with cor pulmonale, had become steadily worse although treated in an oxygen tent and with a mechanical respirator. When he was in deep coma an artificial pneumoperitoneum was induced, a total of 4,000 ml. of air being introduced in the first 6 hours. Rapid improvement occurred, and it was associated with a marked fall of the carbon dioxide combining power of the blood.

Keith Ball

2000. The Pulmonary Artery in Bronchiectasis

W. G. GOBBEL, J. GORDON, and G. J. DIGMAN. *Journal of Thoracic Surgery* [J. thorac. Surg.] **21**, 285-390, April, 1951. 4 figs., 13 refs.

In this study of the pulmonary artery in bronchiectasis human lungs removed at operation or necropsy were examined radiologically after injecting iodized oil into the pulmonary artery and bronchi. It was found that the pattern of the pulmonary artery showed no departure from normal in cases of non-tuberculous bronchiectasis; in tuberculosis, however, the arterial pattern was markedly altered, many of the larger branches being shortened, narrowed, and irregularly distributed, while the smaller branches were reduced in number in areas of fibrosis and absent from areas of caseation. In these tuberculous

cases the arterial pattern was not affected by the presence of tuberculous bronchiectasis.

Although the blood flow through the pulmonary arteries in areas of bronchiectasis has not been studied by the authors, they assume that because the vascular pattern is normal the blood flow too is normal. As ventilation is reduced in the diseased area oxygenation is defective and the arterial oxygen saturation is therefore reduced. The improvement in arterial oxygen saturation which follows resection of the bronchiectatic area is thought to be due to the removal of the poorly ventilated but adequately circulated diseased area, which is acting as a venous-arterial shunt mechanism.

The presence of normal arterial oxygen saturation at rest in cases of fibro-caseous pulmonary tuberculosis with considerable lung destruction is attributed to the defective pulmonary artery circulation in the poorly ventilated areas.

F. J. Sambrook Gower

2001. Concentration of Penicillin in the Lungs. Effects of Two Penicillin Esters in Chronic Pulmonary Infections

A. G. S. HEATHCOTE and E. NASSAU. *Lancet* [Lancet] **1**, 1255-1257, June 9, 1951. 4 figs., 4 refs.

The authors record their experiments with intramuscular L.G.1 (benzylpenicillin diethylaminoethylester hydriodide) and L.G.2 (hydrochloride of benzylpenicillin diethylaminoethylester) in the treatment of a small series of cases of chronic suppurative pulmonary conditions. The dosage given was 1,000,000 units every 12 hours. Control cases received the same dosage of sodium penicillin or procaine penicillin. The course of treatment lasted 1 week in each case. Sputum was either obtained 2, 4, and 6 hours after the injection and assayed for penicillin, or collected over 24 hours, measured, homogenized, and assayed. The assay method used was a modification of the Heatley plate method, using *Sarcina* 1001 as test organism and a standard penicillin solution of 0.1 unit per ml.

Significant amounts of penicillin were found to be excreted in the sputum of patients treated with L.G.1 and L.G.2. The penicillin levels attained in the sputum varied considerably in different patients. With L.G.1 as much as 2.5 units per ml. was found 2 hours after the injection, and up to 0.7 unit per ml. at 6 hours. With sodium penicillin one patient's sputum contained 0.7 unit per ml. at 2 hours, but no penicillin was detected in any patient's sputum at 6 hours. With procaine penicillin the highest penicillin level recorded was 0.06 unit per ml., reached at 4 hours.

No toxic side-effects were observed in any patient treated with L.G.1. In 2 patients treated with L.G.2 allergic symptoms developed. The volume of sputum was considerably reduced in all cases and the patients were benefited by the treatment.

Margaretha Adams

2002. The Treatment of Pneumonia with Bacitracin

E. H. REISNER, F. N. BAILEY, and E. APPELBAUM. *Annals of Internal Medicine* [Ann. intern. Med.] **34**, 1232-1242, May, 1951. 3 figs., 9 refs.

At Bellevue Hospital, New York, 14 cases of acute pneumococcal pneumonia were treated with bacitracin in doses of 30,000 to 99,000 units 6-hourly for 2½ to 12 days: 2 patients were young adults; the others were middle-aged. Of the total, 12 patients recovered, the temperature falling by crisis in 7, 1 patient died, and 1 failed to respond. Pleural effusions occurred in 2 cases. In all the patients there was slight reversible renal damage.

The authors conclude that bacitracin is effective in pneumococcal pneumonia, but should be used only when penicillin and other agents are ineffective.

[A statistical analysis of the results is not presented.]

A. Gordon Beckett

2003. Aureomycin and Penicillin in the Treatment of Bacterial Pneumonia: A Comparative Study

J. L. LELAND and N. ALLEBACH. *New York State Journal of Medicine* [N. Y. St. J. Med.] **51**, 1159-1162, May 1, 1951. 1 fig., 8 refs.

A series of 76 patients admitted to the Bellevue Hospital, New York, with bacterial pneumonia were divided arbitrarily into two groups: 36 received penicillin and 40 aureomycin. The clinical diagnosis was supported by radiological and pathological investigations.

The aureomycin-treated group received an initial dose of 2.0 g. followed by 1.0 g. 6-hourly until defervescence, then 0.5 g. 6-hourly until afebrile. One severely ill patient was given 400 mg. intravenously 8-hourly for 24 hours, and thereafter the usual oral dosage was maintained. Penicillin was given in 500,000-unit initial doses followed by 250,000 units twice daily until the patient had remained afebrile for 2 to 3 days; 1 received more and 1 less than this dose, while 3 received no initial loading dose. [The preparation of penicillin is not specified.] In 5 cases more than one antibiotic was given.

Of the aureomycin group 43% were over 60 years old, against 11% of the penicillin group; 50% of the aureomycin and 36% of the penicillin group had significant pre-existing disease; and treatment was initiated early in 47% of the aureomycin and 62% of the penicillin group. Pneumococci were isolated and typed in 12 of the aureomycin group (18% had bacteraemia) and 15 of the penicillin group (10% had bacteraemia), while there were 4 staphylococcal and 2 "suppurative" (mixed flora) infections in the aureomycin group.

Despite these differences, the authors found that the temperature response and incidence of complications were the same in the two groups. One patient, treated successively with aureomycin, penicillin, and streptomycin, died; necropsy revealed staphylococcal pneumonia, with abscess formation, and advanced pyelonephritis. In regard to toxicity, 35% of those treated with aureomycin suffered nausea, vomiting, or diarrhoea; there were no toxic effects from penicillin therapy.

R. S. Stevens

2004. Treatment of Idiopathic Spontaneous Pneumothorax

F. A. HUGHES and C. C. LOWRY. *Journal of the American Medical Association* [J. Amer. med. Ass.] **146**, 244-247, May 19, 1951. 4 figs., 9 refs.

During the last 3 years 47 cases of spontaneous pneumothorax have been seen at the Kennedy Hospital in Tennessee. These occurred in 40 patients. The average age was 28 years and all but one of the patients were men. In most cases there was no relationship to severe exertion. All the patients complained of the sudden onset of pleuritic pain, which gradually subsided over a few hours to a dull ache and was usually accompanied by dyspnoea. Thoracoscopy in the earlier cases seldom revealed the site of the leak.

Treatment is by obtaining rapid expansion of the lung, and the authors consider that an intercostal catheter connected to an underwater seal is the best means of ensuring this. This treatment was carried out in 30 cases, the catheter being introduced high in the axilla and left in place for 3 to 4 days. There were 3 failures—2 due to a persistent leak from a large bulla which necessitated thoracotomy, and one in a pneumothorax which had been present for 2 months and which required decortication. In 10 instances the pneumothoraces were small and the lung expanded rapidly without therapy, and in 4 cases only needle aspiration was required. Bullae were demonstrated radiologically in 3 patients and a thoracotomy was performed. In the 22 patients who have been followed up for 1 to 3 years there has been no recurrence and no underlying lung disease has developed.

R. Lambert Hunt

2005. Bronchoscopy in the Treatment of Spontaneous and Traumatic Pneumothorax

M. RUBIN and E. H. RUBIN. *Journal of Thoracic Surgery* [J. thorac. Surg.] **21**, 377-384, April, 1951. 4 figs.

In this paper 4 cases are described—2 of spontaneous non-tuberculous pneumothorax and 2 of traumatic haemopneumothorax. In each case atelectasis interfered with re-expansion of the lung and absorption of the pneumothorax. Bronchoscopy revealed viscid plugs of sputum in the bronchi to the affected lobe or lobes, and the removal of these plugs by suction resulted in rapid clinical improvement and absorption of the pneumothorax.

The authors stress the importance of keeping the bronchi clear of secretions, and recommend bronchoscopy in any case in which attempts to obliterate the pneumothorax space are resisted and in which there is radiological evidence of atelectasis.

F. J. Sambrook Gower

2006. Morphological and Functional Aspects of Fibrothorax in Relation to Pathogenesis. (Aspetti morfologici e funzionali del fibrotorace in rapporto alla patogenesi)

C. SCHIZZEROTTO. *Archivio dell'Ospedale al Mare* [Arch. Osp. Mare] **3**, 3-50, Sept., 1951. 20 figs., bibliography.

Digestive Disorders

2007. **Needle Biopsy of the Liver. VII. Observations in Fatty Vacuolization of the Liver**
H. ULEVITCH, E. A. GALL, E. L. ABERNATHY, and L. SCHIFF. *Gastroenterology* [Gastroenterology] 18, 1-7, May, 1951. 6 figs., 6 refs.

In a series of 750 needle biopsies of the liver the authors encountered 26 patients in whom fatty infiltration of the liver was the sole histological abnormality. Frequent findings in these 26 cases were excessive alcohol consumption, poor nutrition, nausea and vomiting, and hepatic pain. The liver was tender in 7 and enlarged in only 16. Liver function tests were of little value, except bromsulphalein retention, which was abnormal in 15 out of 17.

[This article would have gained in interest if the various findings had been related to the degree of fatty change.]

Richard Terry

2008. **The Treatment of Alcoholic Addiction with "Antabuse": Observations on a Group of Patients with Nutritional Liver Disease**

T. H. HURLEY. *Proceedings of the Royal Australasian College of Physicians* [Proc. roy. Aust. Coll. Phys.] 6, 71-82, Jan., 1951. 14 figs., 10 refs.

The author has assessed the toxic effects of "antabuse" (tetraethylthiuram disulphide) in anorexic alcoholics suffering from dietary deficiency and in whom there was evidence of reversible or irreversible liver damage. The progress of the patients was followed by serial biochemical examinations (serum bilirubin concentration; cephalin flocculation; serum albumin, globulin, and alkaline-phosphatase concentration) and liver biopsies.

He concludes that antabuse has no detectable effect on the recovery of alcoholic patients with fatty livers. In 2 cases observed during 6 months' administration of antabuse there was no evidence of liver damage caused by the therapy.

B. G. Maegraith

2009. **The Syndrome of Myopathic Occlusion of the Upper End of the Oesophagus.** (Le syndrome d'occlusion myopathique de la bouche de l'oesophage)

A. FAVROD-COUNE. *Revue de Laryngologie, Otologie, Rhinologie* [Rev. Laryng., Bordeaux] 72, 112-137, March-April, 1951. 9 figs., 24 refs.

The syndrome of myopathic occlusion of the upper end of the oesophagus was first described by Montandon in 1948. He called it a permanent pseudo-spasm of the oesophagus. The author has studied 3 cases in detail to appraise the mechanism producing the symptoms. The study of the act of deglutition is difficult. It is a complex act with a rapid sequence of events which are complicated by violent reflexes occurring in the upper segment of the digestive tube. As a result of his study the author concludes that the syndrome of spasm is based with few exceptions on a well-defined anatomical factor. Apart

from neighbouring inflammations such as spondylarthritis, it is possible to find an interstitial fibrosis, a degeneration of the neuromuscular plexus, or even a muscular atrophy of the pharyngo-oesophageal segment. These different histological changes give rise to dysphagia due not to spasm, but to achalasia—defective muscular relaxation: they have been described by Mosher, Macmillan, Worms, and Montandon. It is essential to study in more detail the precise function of the sympathetic and parasympathetic supply and the local reflexes concerned in the disordered muscular contraction and relaxation when these local lesions develop. Dysphagias of this type are very complex and often difficult to understand.

E. D. Dalziel Dickson

STOMACH

2010. **Retrograde Extrusion or Prolapse of the Gastric Mucosa into the Esophagus**

M. FELDMAN. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 222, 54-60, July, 1951. 4 figs., 3 refs.

Wells (*Amer. J. Roentgenol.*, 1947, 58, 194) published the first description of this condition. In his patient the prolapse appeared to result from a small hiatal hernia. Barium-meal examination showed the oesophagus to be slightly dilated and completely blocked. The lower end of the barium column was scalloped, and on oesophagoscopy the scalloped appearance was found to be due to normal gastric mucosa.

Two further alleged cases are now presented from a purely radiological viewpoint. When the patients were tilted into the prone position "a sliding knuckle of gastric mucosa could be seen extruding up into the lumen of the lower oesophagus". [The criteria for differentiating between this appearance and that of hiatal hernia are open to question. The pathognomonic finding of blockage of the oesophagus was apparently not sought, and there is no mention of oesophagoscopy. The clinical course is also not described.] Retrograde prolapse is said not to occur at necropsy, and, apart from Wells's case, to be unknown to the endoscopists.

Denys Jennings

2011. **Prolapse of the Gastric Mucosa through the Pylorus with Concomitant Gastrointestinal Pathology**

E. M. RAPPAPORT, E. O. RAPPAPORT, and A. STANTON. *Review of Gastroenterology* [Rev. Gastroent.] 18, 473-487, July, 1951. 11 figs., 16 refs.

Prolapse of the gastric mucosa is commoner than is generally supposed. It is a purely radiological diagnosis, and there is no clinical evidence that it causes symptoms. Cases are reported in which prolapse occurred in combination with gastric and duodenal ulcers, gastric car-

cinoma, pancreatic carcinoma, and hiatus hernia. Prolapse was also seen in cases of infective hepatitis, cirrhosis of the liver, chronic cholecystitis with and without gallstones, intestinal obstruction, *Salmonella* infections, amoebic granuloma of the caecum, diverticulitis of the sigmoid, and ulcerative colitis. In each case the symptoms were the classical ones of the associated disease, and there was nothing to suggest that the existence of the prolapse modified the clinical picture. In one patient the symptoms persisted unchanged despite pyloroplasty and removal of the prolapsing mucosa. On the evidence available it is believed that prolapse can occur without the antral mucosa being inflamed.

The bibliography includes 3 papers by the same authors which are "in publication".

Denys Jennings

2012. Studies on the Cephalic Phase of Gastric Secretion in Normal Subjects and Ulcer Patients

O. NORING. *Gastroenterology* [*Gastroenterology*] 18, 413-418, July, 1951. 2 figs., 22 refs.

Recent advances in psychosomatic medicine have shed a new light on the aetiology of peptic ulcer, and increasing importance is being attached to "psychic" factors. Accordingly particular interest has been shown in the "psychic" (cephalic) phase of gastric secretion. Palmer and Levin (*Gastroenterology*, 1949, 13, 83) maintain that reflexes operating through the vagus nerve constitute an essential cause of hypersecretion. Most investigators have been concerned with the nocturnal fasting secretion of normal subjects and patients with peptic ulcers, while paying little attention to the purely cephalic phase. Only Necheles and Maskin (*Amer. J. digest. Dis.*, 1936, 3, 90) appear to have attempted the experimental study of cephalic secretion—that excited by sham feeding. However, their sham-feeding test (chewing an orange) appeared to be mildly irritant.

In the present paper the author reports his own investigations on 42 normal subjects, 53 patients with duodenal ulcer, and 7 with gastric ulcer in the surgical department of the Rigshospitalet, Copenhagen. The patients came fasting to the laboratory in the morning. A fine-calibre duodenal tube was introduced through the nose (after painting with cocaine) into the stomach, which was emptied at once and again after 10 minutes, thus providing two fasting samples. Then the patient was given 2 or 3 buttered black-bread sandwiches with various sandwich spreads to chew, swallowing being carefully avoided and the chewed food returned to a bowl. The gastric secretion was aspirated every 10 minutes until the increase in secretion had ceased. The acidity was titrated and the total chloride and pepsin content estimated.

The patients with duodenal ulcer showed a more marked dispersion in the quantity of secretion and maximum acidity, as well as a higher volume of secretion, than normal subjects. There was no significant difference between the average acidity, chloride content, and pepsin value in the two groups. The patients with gastric ulcer had a lower acidity and lower chloride and pepsin content in their secretion, whereas its volume was midway between the volumes registered in the other two groups. Acidity

curves showed a more prolonged increase in patients with duodenal ulcer than in normal individuals.

E. Forrai

2013. Prognosis of Healed Gastric Ulcers

B. BARSBY. *Lancet* [*Lancet*] 2, 59-61, July 14, 1951. 2 figs., 1 ref.

In this paper from a London hospital is reported a 5-year study of the recurrence rate in cases of gastric ulcer after initial healing had been confirmed gastroscopically. The patients were highly selected, as all those with definite indications for surgery were excluded, including those whose lesion failed to heal after a strict course of medical treatment in hospital.

A total of 56 cases were treated: in 22 there was recurrence and in 20 the ulcer remained healed; 14 patients did not receive adequate treatment. The commonest period of recurrence was in the first 6 months; and in this group as a whole there was a much longer history of past ulcer symptoms than in those cases in which the ulcer did not recur. Attempts were made to follow up the cases at 3-monthly intervals, and gastroscopy was performed initially and at regular intervals to observe the progress of healing. No case was included unless gastroscopic evidence of healing was obtained.

Of the 42 patients who were followed up after complete healing of the ulcer had been demonstrated gastroscopically, in 43% the ulcer recurred in the original site and in 9% in a new site. It is concluded that the prognosis in a case where the ulcer heals rapidly (within 6 weeks) with a deep scar is worse than in one where the ulcer heals slowly with only a minimal scar.

Gastric acidity seemed to have no close relationship to the prognosis, and histamine-fast achlorhydria was found in cases in both groups. It was found that 10 out of 14 patients who had received inadequate treatment still had active ulcers, and although some of the ulcers in this group were acute they all became chronic, sometimes in as short a time as 3 months.

The author suggests that patients should receive medical treatment in hospital until it has been shown gastroscopically that the ulcer has healed and it is possible to tell from the type of healing observed whether the ulcer is likely to recur.

I. McLean-Baird

2014. Studies on Pepsin Secretion—I. Nocturnal and Hypoglycemic Secretion in Patients with Duodenal Ulcer and without Gastro-intestinal Disease

A. B. CHINN, D. T. BOOK, and A. J. BEAMS. *Gastroenterology* [*Gastroenterology*] 18, 427-437, July, 1951. 5 figs., 7 refs.

The acid concentration of gastric secretion is known to be usually high in peptic, and particularly duodenal, ulceration. Results of investigations into the concentration of pepsin have, however, shown some disagreement. Consequently the present authors, working in the Department of Medicine, Western Reserve University, have studied pepsin concentration and the occurrence of pepsin inhibitors. For this purpose the pepsin content was estimated in samples of nocturnal gastric secretion and of gastric secretion aspirated after insulin-induced

hypoglycaemia from patients with duodenal ulceration and subjects without ulceration. They found that nocturnal gastric secretion and that induced by insulin hypoglycaemia are greater in volume and contain more free hydrochloric acid in patients with duodenal ulcer than in persons with no gastro-intestinal disease. There was, however, no significant difference in the pepsin content per unit of volume of either the nocturnal gastric secretion or that following insulin between the patients with duodenal ulcer and the control group. Neither the nocturnal gastric secretion from the duodenal-ulcer group nor that from the control subjects contained inhibitory substances to crystalline pepsin activity. In most subjects of both groups there was no real difference in the capacity per unit of volume of gastric juice to produce proteolysis. In patients with duodenal ulcer, however, though they secrete a larger total volume, the duodenal mucosa might be exposed to uninhibited acid-pepsin solution more frequently than occurs in normal subjects. It seems quite possible that by this mechanism the factor of total volume may play an important part in the genesis, prolongation, and recurrence of duodenal ulceration.

E. Forrai

2015. A Study of the Changes in pH of Gastric Contents in Peptic Ulcer using the Twenty-four Hour Test Meal
G. WATKINSON. *Gastroenterology* [*Gastroenterology*] **18**, 377-390, July, 1951. 10 figs., 7 refs.

In this paper from the Department of Medicine of the University of Leeds the author reports upon the 24-hour gastric analyses which he carried out to investigate the changes in pH of the gastric contents under liberal dietary conditions in 20 normal subjects and 60 patients with peptic ulcer on whom some 120 tests were performed. The 24-hour test-meal examination was originally devised by James and Pickering (*Clin. Sci.*, 1949, **8**, 181); these authors, however, paid no attention to the site or stage of healing and dismissed the possible significance of duodenal regurgitation.

The present author's method was as follows: A Ryle tube was passed at the beginning of the test and the position of the tip was checked radiologically. The patient received a liberal gastric diet, 2-hourly milk feeds being administered from 6 a.m. to 10 p.m. Specimens of gastric contents measuring 10 to 20 ml. were aspirated half-hourly or hourly by day and hourly by night, and the pH of unfiltered specimens was estimated by means of the sealed glass electrode. The presence of bile staining was also recorded. The results show that the mean nocturnal acidity in duodenal ulcer is significantly higher than normal, while mean acidity values in gastric ulcer are significantly lower than normal. Falls in the pH almost to alkaline levels were observed during the night in 12 out of 25 cases of gastric ulcer studied. The site of the ulcer and the stage of healing have been shown to affect the degree of nocturnal neutralization in many cases. Although the factor of duodenal regurgitation was dismissed by James and Pickering, the consistent finding of bile staining in all cases showing nocturnal neutralization in the present study appears to be significant.

E. Forrai

2016. The Clinical Response of Patients with Peptic Ulcer to a Topical Mucigogue (Eugenol)

J. BANDES, N. A. SAMUELS, F. HOLLANDER, R. L. GOLDFISCHER, and A. WINKELSTEIN. *Gastroenterology* [*Gastroenterology*] **18**, 391-399, July, 1951. 16 refs.

Opinions seem to differ on the subject of the protective value of the mucus secretion of the stomach. The authors of this paper from the Mount Sinai Hospital, New York, have conducted a series of experiments to determine whether a suitable mucus-stimulating agent will give increased protection to the mucosa in peptic ulcer and thus affect the clinical course. It had previously been shown (Hollander and Lauber, *Proc. Soc. exp. Biol.*, N.Y., 1948, **67**, 34) that an aqueous emulsion of eugenol is highly effective as a mucigogue when applied topically to the gastric mucosa.

In the present investigations 3% eugenol emulsion was given twice a week for 3 weeks to 14 patients with active symptoms of gastric or duodenal ulceration which persisted despite the usual ulcer regimen. There were 3 unequivocal failures; one other case could not be classified at the time. The remaining 10 patients experienced complete or partial relief, which lasted a year or more in some instances. There was no correlation between clinical response and laboratory findings as assessed by x-ray examination and acidity curves. Because of this and also because the patients' statements could not be relied upon, the authors were unable to demonstrate any unequivocal beneficial effect of eugenol therapy on the clinical course in the cases studied. However, the suggestion is made that if prolonged stimulation of mucus secretion in the region of the ulcer could be assured by the use of a less irritating mucigogue which did not have to be removed the therapeutic effects of mucus stimulation might be more pronounced than those obtained.

E. Forrai

See also Radiology, Abstract 1851.

INTESTINES

2017. Chronic Ulcerative Colitis—Clinical and Bacteriologic Response to Aureomycin

M. H. STREICHER and R. KNIERING. *American Journal of Digestive Diseases* [*Amer. J. digest. Dis.*] **18**, 231-234, July-Aug., 1951. 17 refs.

A daily dose of 3 to 6 250-mg. capsules of aureomycin was administered orally to 18 men and 32 women. [The duration of treatment is not stated.] There were 23 cases in the chronic stage and 27 in the acute stage. The majority of the patients "were hospitalised for 2 weeks and controlled during the experimental trial". The study was carried on for one year. All except 13 of the patients complained of side-effects. The commonest complaint was nausea or vomiting; in 6 patients there was itching or a skin rash.

The numbers of *Bacterium coli*, staphylococci, and streptococci per gramme of faeces were all reduced. The proctoscopic changes after treatment "were not sufficiently pronounced to evaluate", but the stools became

more formed. The impression was that the discomfort in the abdomen was alleviated and the number of evacuations reduced.

Denys Jennings

2018. Potassium Deficiency in Ulcerative Colitis

M. LUBBRAN and P. M. MCALLEN. *Quarterly Journal of Medicine [Quart. J. Med.]* 20, 221-232, July, 1951. 2 figs., 38 refs.

In 4 out of 30 consecutive cases of ulcerative colitis a severe deficiency of potassium, together with electrocardiographic changes and profound muscular weakness (3 cases), was observed in the acute phase of the disease. In one female patient aged 44 years, who had a prolonged exacerbation of ulcerative colitis with serum potassium value falling to 2.05 mEq. per litre, potassium and sodium balance studies were carried out during two periods (8 months apart). On normal diet there was an excessive loss of potassium in the faeces (approximately 1 to 2 g. of potassium during 24 hours) and a markedly negative potassium balance; the potassium balance promptly became positive on supplementation with 16 to 24 g. of potassium chloride daily. On all intakes of potassium there was a rough parallelism between the excretion of potassium and sodium individually and the volume of faeces each day, but there was a much closer linear relationship between the sum of potassium and sodium concentrations and the faecal volume; the mean concentration of these electrolytes in the faeces was 107.5 mEq. per litre, which is 70% isotonic. The urinary excretion of potassium was consistently very low; the excretion of sodium was also remarkably high in the faeces and low in the urine, but the sodium balance was positive in the first study period and negative in the second. When a dose of 8 g. of potassium chloride in 700 ml. of water was given, the serum values showed rapid absorption of potassium such as is found in normal subjects; an oral sodium-tolerance test produced no change in the serum level of sodium. The glucose-tolerance test and the fat balance showed normal absorption. The muscular weakness was improved when 12 g. of potassium chloride in divided doses was given daily, but it recurred each time the potassium chloride was discontinued; the greatest subjective benefit was obtained when the daily dose of potassium chloride was increased to the limit of the patient's tolerance (24 g. of potassium chloride in divided doses daily).

It is concluded that the main determinant of the degree of electrolyte loss is the volume of the faeces.

Joseph Parness

2019. Reversibility in Ulcerative Colitis. Clinical and Roentgenologic Observations

J. B. KIRSNER, W. L. PALMER, and A. P. KLOTZ. *Radiology [Radiology]* 57, 1-14, July, 1951. 11 figs., 3 refs.

The main theme of this paper is the remarkable curability of ulcerative colitis. Many case records with reproductions of radiographs are presented to show that the disease may heal clinically and that the radiological appearances also may become normal. In a few cases clinical cure was complete, although the classical

radiological picture of ulcerative colitis persisted. In other cases described, even gross scarring and stricture formation disappeared in the course of conservative management. No specific therapeutic scheme was responsible for these good results, although successful psychotherapy, chemotherapy, and the administration of ACTH seemed, in individual cases, to launch the healing process. The main therapeutic desiderata appear to be prolonged rest, correct nutrition, relief of emotional tension, and an attitude of patience and hope on the part of physician and sufferer.

[This is an interesting and well-illustrated paper, and the facts presented lend considerable support to such a doctrine of hopefulness and conservatism.]

J. Naish

2020. Treatment of Ulcerative Colitis

W. J. GRACE and H. G. WOLFF. *Journal of the American Medical Association [J. Amer. med. Ass.]* 146, 981-987, July 14, 1951. 6 figs., 21 refs.

In this study an unselected group of 19 patients with chronic non-specific ulcerative colitis were treated by psychotherapy. The patients were found to be very dependent on the approval of others: if they could not be "nice to everyone" they became anxious and tense. Their inability to tolerate hostility in others and to express or act out their own hostility, their incapacity to make decisions, and their passivity made for ever-increasing conflict. They were often frustrated and humiliated, but could not give vent to their anger, and the anxiety from this conflict provoked exacerbations of symptoms. The patients were hostile but "sweet", anxious but "calm", timid yet rebellious. They had aggressive fantasies, but their behaviour was passive. They experienced strong guilt feelings about their hostility and felt unworthy of the regard of others.

Treatment was carried out by interviews at intervals of a few days or weeks. The core of the method was the establishment of a constructive physician-patient relationship. The patient was encouraged to express, with a free show of feeling, to a sympathetic and appreciative physician, the major complaints and difficulties in his life situation. The interviews were directed towards bringing about in the patient an understanding of himself and helping him to adopt a more appropriate attitude towards his life and the people in it. Rearrangement of the patient's environment, when this was feasible, was attempted. No medication was employed in any of the patients.

Eleven patients showed substantial improvement, and 4 of these became free of symptoms and remained so for more than a year; 2 improved slightly; and 9 did not improve at all. There was no correlation of age, duration of illness, or severity of illness with degree of improvement; the chief factor in prognosis was the patient's capacity to participate in the therapeutic relationship with the physician. The results of psychotherapy seem to be at least as effective as those claimed by other authors for medical treatment, and this suggests that the same principle also governs the treatment of ulcerative colitis by physical means.

Desmond O'Neill

Endocrinology

EXPERIMENTAL

2021. Investigation of the Effect of Adrenal Cortical Hormone on Thyroid Function by means of Radioactive Iodine. (Die Wirkung von Nebennierenrindenhormon auf die Funktion der Thyreoidea, untersucht mit J^{131}) F. VERZÁR and V. VIDOVIČ. *Helvetica Physiologica et Pharmacologica Acta* [*Helv. physiol. pharmacol. Acta*] 9, 214-221, 1951. 3 figs., 15 refs.

The literature pertaining to the functional relationship between the adrenal and thyroid glands is briefly reviewed. Rats of 200 to 250 g. body weight received 0.05 mc. radioactive iodine in 0.5 ml. physiological saline by intraperitoneal injection. The Geiger counter tube was covered with a lead shield perforated by a 3.5-mm. hole. Each animal was anaesthetized with ether and tied down on its back, and counts were made over the place of injection and over the thyroid in the neck. In normal rats the dose of J^{131} was found to accumulate in the thyroid in 16 to 24 hours.

The capacity to concentrate the isotope was found to be diminished by 2.5 mg. cortisone acetate twice daily, by 2.5 to 5 mg. deoxycortone acetate twice daily, or by adrenal cortical extract ("eschatin", 0.5 ml. twice daily). The release of J^{131} from the thyroid was also diminished by these hormones. After adrenalectomy the capacity of the thyroid to concentrate iodine was no smaller than in controls; indeed, in most cases the uptake was greater.

The physiological significance of the observations is discussed.

Norval Taylor

2022. Influence of Thyroxine on the Desensitising Action of ACTH and of Cortisone in B.C.G.-infected Guinea-pigs

D. A. LONG, A. A. MILES, and W. L. M. PERRY. *Lancet* [*Lancet*] 1, 1392-1394, June 30, 1951. 3 figs., 3 refs.

Albino guinea-pigs in groups of 5 to 15 were given 2 mg. wet weight of B.C.G. vaccine intramuscularly and were tested for sensitivity 28 days later with tuberculin by a multiple-dose method. The animals were maintained on an ascorbic-acid-free basic diet, the vitamin being supplied by unlimited cabbage. The diameter of the tuberculin lesions after 24 hours was found to be proportional to the logarithm of the dose. By plotting the mean lesion diameter against the logarithm of the dose the position of the dose-response curve may be used to estimate the degree of sensitivity developed by the guinea-pigs.

A dose of 50 mg. propylthiouracil by mouth thrice weekly for 4 weeks had no effect on sensitivity by itself, but inhibited the desensitizing action of a single dose of cortisone (2 mg.) or of ACTH (1 international unit). A 28-day course of thyroxine, sufficient to produce a mild thyrotoxicosis, caused a significant increase in

sensitivity. If the thyroxine was given in an amount which did not cause any signs of thyrotoxicosis, it had no effect on the hypersensitivity, but it restored the desensitizing action of cortisone and ACTH in propylthiouracil-treated guinea-pigs. It was concluded that thyroxine was necessary for the desensitizing action of cortisone and ACTH.

Norval Taylor

2023. The Influence of Adrenaline and Deoxycortone on the Behaviour of Eosinophil Leucocytes in the Normal and in the Adrenalectomized White Rat. (Der Einfluss des Adrenalins und des Desoxycorticosterons auf das Verhalten der eosinophilen Blutzellen der normalen und der epinephrektomierten weissen Ratte)

F. HENI and H. MAST. *Zeitschrift für die Gesamte Experimentelle Medizin* [*Z. ges. exp. Med.*] 117, 282-287, 1951. 3 figs., 14 refs.

Subcutaneous injections of 15 μ g. of adrenaline were given to 15 normal rats. In all animals a pronounced diminution in the number of circulating eosinophil leucocytes was noted. The average decrease was more than 90% of the initial value within 4 hours. The fall did not begin immediately after the injection of adrenaline, in fact there was a slight increase in circulating eosinophils during the first hour. Adrenalectomy was carried out on 20 rats, and 4 days later 50 μ g. of adrenaline was injected subcutaneously. In 12 of the rats there was no fall in the eosinophil count; on the contrary, within 3 hours the average eosinophil count had risen by 76% of its initial value. On the following day, 13 of the animals which had shown no fall in eosinophil leucocyte count after adrenaline were given deoxycortone intravenously. The results were inconsistent. Five animals, of which 3 died, showed a fall in eosinophil leucocyte count; the remaining 8 rats showed no decrease in eosinophil cells.

The authors conclude that deoxycortone has no influence on the eosinophil leucocyte count and that the changes observed are due to vasomotor responses, dilatation of peripheral vessels leading to an increase, constriction and collapse causing a fall, in circulating eosinophil leucocytes.

H. Lehmann

2024. Insulin and the Suprarenal Gland of the Rabbit

G. B. WEST. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] 6, 289-293, June, 1951. 2 figs., 9 refs.

Rabbits of both sexes kept without food overnight were given a dose of insulin sufficient to produce signs of hypoglycaemia. Samples of blood from an ear vein were taken for blood sugar determinations before injection with insulin, and at given times ranging from 1 to 12 hours after the injection. Immediately after the second sample of blood was taken the animals were killed by concussion and bled out. The adrenals were

dissected, weighed, and ground up with sand and 10 ml. 0.1 N hydrochloric acid per gramme. The extracts were filtered and assayed for adrenaline and noradrenaline content by the method of Burn, Hutcheon, and Parker (*Brit. J. Pharmacol.*, 1950, 5, 142). Total activity was measured by its effect on rabbit's isolated ileum. Some assays were performed on the isolated rectum of the chick, the isolated uterus of a non-pregnant rat in dioestrus, or the uterus of a non-pregnant spinal cat.

During the first 2 hours, while the blood sugar level was falling, there was a significant rise in the total activity. This was succeeded by a rapid fall, minimum values being evident 4 hours after insulin and about 1 hour after the maximum reduction in blood sugar level. During the first 2 hours after the injection of insulin, noradrenaline might appear in the gland extract; at all other times only adrenaline was found in the extracts. Recovery to control values occurred in 6 hours, with a small over-compensatory swing evident at 8 and 12 hours, in spite of the fact that the blood sugar level was still below the normal control values.

The conclusion reached was that if noradrenaline is a precursor of adrenaline in the adrenal of the rabbit, then methylation to form adrenaline occurs rapidly, even in an exhausted gland.

Norval Taylor

2025. The Effect of Salicylates on the Pituitary and Suprarenal Glands

B. S. HETZEL and D. C. HINE. *Lancet* [*Lancet*] 2, 94-97, July 21, 1951. 1 fig., 29 refs.

This investigation was undertaken at the Institute of Medical and Veterinary Science, Adelaide, following a recent report of the development of Cushing's syndrome in a patient treated with aspirin (5 g. per day) for rheumatic fever. Experiments have been made to determine whether salicylates in the therapeutic dosage have an effect on the pituitary and adrenal glands (shown by removal of ascorbic acid from the adrenals) and whether this effect could be abolished by hypophysectomy or by preliminary treatment with adrenal cortical hormone (which is known to prevent the normal depletion of ascorbic acid by activity of the pituitary and adrenal glands). Wistar rats were used and the methods employed were all standard surgical and biochemical techniques. Sodium salicylate and sodium *p*-aminosalicylate were administered in amounts adequate to maintain a blood salicylate level of 30 to 40 mg. per 100 ml., which is within the range attained in patients under treatment for rheumatic fever.

Salicylate caused significant depletion of adrenal ascorbic acid even more marked than that due to insulin, which is a known stimulant of the pituitary and adrenal glands; the effect was directly proportional to the dosage. Other sodium salts had a slight action, but not comparable with that of sodium salicylate; calcium acetyl-salicylate and sodium *p*-aminosalicylate were highly active.

Statistical analysis showed no significant difference between the adrenal ascorbic acid of normal rats and that of hypophysectomized rats treated with sodium salicylate, indicating that the mediation of the pituitary

is essential. Preliminary treatment with cortisone tended to inhibit the effect of salicylates.

These results suggest that the beneficial results of salicylate therapy are due to activation of the pituitary and adrenal glands, leading to the production of cortisone-like steroids.

Nancy Gough

2026. The Influence of STH, ACTH, and Cortisone upon Resistance to Infection

H. SELYE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] 64, 489-494, June, 1951. 8 figs., 8 refs.

Evidence has accumulated that ACTH and cortisone can diminish resistance to infection both in experimental animals and man. The mechanisms responsible are not yet clearly understood, but it is possible that the general catabolic effect of the hormones, their inhibitory action upon granuloma formation, and their destructive action upon lymphatic tissues may be involved. The author, having noted that somatotrophic hormone (STH) acts antagonistically to ACTH in these respects, argued that it might be able to increase resistance to infection.

In one experiment, 8 rats were given 10 mg. of cortisone acetate by subcutaneous injection daily for 12 days; 5 died before completing the course; these and 1 survivor had multiple abscesses; all had lost a great deal of weight. A further 9 rats, while receiving the same dose of cortisone, were also given 2 mg. of STH daily; all survived and their average weight was unchanged. The experiment was repeated over a 17-day period with comparable results. In a second experiment cortisone was replaced by ACTH given subcutaneously in 2-mg. doses 6 times daily; 5 out of 7 animals given only ACTH had multiple abscesses, while 7 out of 7 given STH in addition remained healthy.

Microscopically, the animals in which there was abscess formation showed many large bacterial colonies throughout the lungs, kidneys, liver, and spleen (and in 2 cases on the peritoneum and in 1 on the endocardium) with almost no connective-tissue reaction. Identification of the bacteria has not been completed, and it remains to be established whether STH arrests the growth of the true pathogens or only of those normally non-pathogenic organisms whose proliferation is stimulated by an excess of glucocorticoids.

There is a brief discussion of the significance and possible explanations of these findings.

H. McC. Giles

2027. The Effects of 17-Hydroxy-11-dehydrocorticosterone upon the Adrenals of Normal and Hypophysectomized Rats Maintained with Adrenocorticotropin

R. A. LEWIS, E. ROSEMBERG, and L. WILKINS. *Endocrinology* [*Endocrinology*] 47, 414-417, Dec., 1950. 7 refs.

Cortisone acetate (1.25 mg. daily) was injected into normal rats and into hypophysectomized rats maintained on a constant dosage (0.4 mg. thrice daily) of adrenocorticotrophin. The treatment reduced the weight and increased the cholesterol content of the adrenals in the normal rats, but had no such effects in the hypophysec-

tomized animals. This is strong evidence that cortisone produces these effects by reducing adrenocorticotrophin secretion. This would explain the beneficial results that have been reported (Wilkins, Lewis, Klein, and Rosemberg, *Bull. Johns Hopkins Hosp.*, 1950, 86, 249) when cases of adrenal hyperplasia are treated with cortisone.

Peter C. Williams

2028. Oxidation of 11-Desoxycorticosteroids with Adrenal Tissue Homogenates

K. SAVARD, A. A. GREEN, and L. A. LEWIS. *Endocrinology [Endocrinology]* 47, 418-428, Dec., 1950. 4 figs., 9 refs.

11-Deoxycortone or its 17-hydroxy derivative was incubated with a homogenate of the adrenal gland. The total steroids were extracted after the incubation and tested biologically by their capacity to increase the liver glycogen of fasting adrenalectomized mice, and chemically by paper chromatography.

The steroid extract was often toxic, but usually the glycogenic activity was so increased that it could be detected in quantities small enough to be non-toxic. The activity increased rapidly and was greatest after one hour's incubation. The activity produced was increased when ox blood was added to the homogenate; the reason for this is unknown, as ascorbic acid, riboflavin, and glutathione were without effect. The very low glycogenic activity of deoxycortone was not increased when it was mixed with adrenal homogenate only after the latter had been incubated.

The best results were obtained when 30 mg. of deoxycortone acetate was incubated with 25 g. of homogenized adrenal tissue. In similar quantities, incubation of the 17-hydroxy derivative yielded about thrice the amount of glycogenic activity, which agrees with the relative activities of deoxycortone and the 17-hydroxy derivative, suggesting that oxidation had occurred at the C (11) position.

This conclusion is supported by the chromatographic evidence. Glycogenic activity was associated with the appearance of material in the $C_{21}O_4$ zone between the faster moving $C_{21}O_3$ zone, which contained the unchanged deoxycortone, and the slower $C_{21}O_5$ zone, which contained pigmented material probably consisting of oxidized adrenaline or adrenaline-like substances. Most of the glycogenic activity was accounted for when the material in the $C_{21}O_4$ zone was extracted and tested biologically. The identification of the material was confirmed by mixed chromatography of the incubation extract with the pure steroids. Similar evidence confirmed the conversion of the 17-hydroxy-11-desoxycorticosterone to 17-hydroxycorticosterone. Thus the capacity of adrenal tissue to oxidize 11-desoxycorticosteroids at the C (11) position is proved.

Peter C. Williams

2029. Limitations of the ACTH Regulating Effect of Corticoids

C. FORTIER, S. YRARRAZAVAL, and H. SELYE. *American Journal of Physiology [Amer. J. Physiol.]* 165, 466-468, May, 1951. 26 refs.

2030. The Influence of the Adrenal Cortex on Antibody Production *in vitro*

S. ROBERTS and A. WHITE. *Endocrinology [Endocrinology]* 48, 741-751, June, 1951. 2 figs., 28 refs.

In this paper the authors present results which may well be important in explaining the controversial findings of previous investigators. The experimental animal used was the rat. Haemolysin production was stimulated by the injection of 0.5 ml. of a 2% suspension of sheep erythrocytes. Three groups of animals were used: normal intact controls, rats which had previously been adrenalectomized, and intact rats which received injections either of ACTH or of adrenocortical extract.

In a first series of experiments the authors examined the production of haemolysin in the serum and in various organs of the intact animals. Maximum production of haemolysin occurred about 5 or 6 days after the injection of the erythrocytes, and there appeared to be no significant difference between the control and experimental groups at this time. However, in the mesenteric lymph nodes and in the thymus gland there was little haemolysin present on the 4th day after injection in the adrenalectomized group, although in the other two groups it was present in considerable quantity. On the other hand, much more striking effects were observed when the spleen was removed from the animals, minced, and incubated in a Warburg apparatus. Under these conditions it was found that the spleens of adrenalectomized animals produced practically no haemolysin, whereas those of the control animals produced a considerable amount. The spleens of animals which had received injections of adrenocortical extract or of ACTH produced very much larger amounts than the spleens of control animals.

In order to elucidate the reasons for the different results obtained in intact animals and *in vitro* the authors studied the uptake of haemolysin by various organs incubated in serum containing this antibody. They found that the uptake was considerably influenced according to whether the organ concerned had been removed from a normal control animal, from a previously adrenalectomized animal, or from an intact animal which had been treated with adrenocortical extract or with ACTH. So far as lymphoid tissue, liver, and kidney were concerned there was considerably less uptake of the haemolysin when these organs had been removed from an adrenalectomized animal than when they had been removed from a control animal. Conversely, when the animal from which they came had previously been treated with adrenocortical extract the uptake was considerably greater than in the control.

It is suggested, therefore, that the failure to observe any considerable difference in the serum level of antibody in the various groups of animals arises from the fact that adrenocortical hormones cause both an increased rate of production of antibodies and an increase in their removal from the circulation. The serum level is a result of these two factors, and may remain the same even though the turnover of antibody is much greater in intact and in ACTH-treated animals than in those which have been adrenalectomized. The authors suggest that this may be only one specific example of a more general pheno-

menon—that of the dynamic interchange of protein between tissues and plasma, which has previously been shown to be influenced by pituitary-adrenocortical secretion.

G. A. Smart

THYROID GLAND

2031. **Atypical Facial Neuralgia in the Hypothyroid State**
F. B. WATTS. *Annals of Internal Medicine* [Ann. intern. Med.] 35, 186–193, July, 1951. 5 refs.

The author describes 29 cases of atypical facial neuralgia with vague pains about the face and neck, often associated with recurrent headache and precordial pain. [The evidence for a diagnosis of hypothyroidism is not very convincing, although one patient had a basal metabolic rate as low as -27% .] In all cases the condition improved within 2 weeks with thyroid extract in doses of the order of $\frac{1}{2}$ gr. (16 mg.) thrice daily.

G. S. Crockett

2032. **Function of the Adrenal Cortex in Myxedema, with Some Observations on Pituitary Function**

H. STATLAND and J. LERMAN. *Journal of Clinical Endocrinology* [J. clin. Endocrinol.] 10, 1401–1416, Nov., 1950. 2 figs., 20 refs.

Primary hypothyroidism might be expected to depress other endocrine function by reducing the metabolism of the glands concerned. If the pituitary were affected in this way it would in turn affect other endocrine glands, but there is also the probability that its function would be stimulated by thyroxine deficiency, so that a variety of general effects is possible.

These possibilities as they affect adrenal and pituitary function were investigated in 43 hypothyroid patients, who were carefully selected to exclude any with evidence that the condition was of pituitary origin. Adrenal androgen secretion appeared to be subnormal in untreated cases; the average daily 17-ketosteroid excretion was 4.8 mg. in the men and 2.3 mg. in the women. After treatment the average output in the pre-menopausal women was doubled, but that in the men and post-menopausal women increased little, if at all. The secretion of corticoids influencing electrolyte balance and general metabolism was more rarely abnormal. Blood electrolyte concentrations were within normal limits, though in a small series of cases where these were measured before and after treatment there was a small rise in the sodium concentration and a fall in that of potassium. The results of a salt-deprivation test were normal in 5 cases, but provoked Addisonian crises in 2; one of these 2 patients probably had co-existing Addison's disease, but the other gave a normal test response when treated with thyroid. Insulin-tolerance curves showed a delayed fall (insulin resistance) and recovery (hypoglycaemia unresponsiveness), with a restoration to normal after thyroid treatment. The abnormal curves might be due to sluggish circulation and reduced metabolism rather than to specific endocrine causes. The 11-oxy corticosteroid excretion and the eosinophil-cell response to adrenaline injection were at the lower limit

M—2M

of normal variation, but showed little change after treatment. Urinary gonadotrophin excretion tended to be normal in the men and pre-menopausal women, but subnormal in post-menopausal women; where this was changed by thyroid treatment, an increase was more common than a decrease. One woman with a low excretion and amenorrhoea, suggesting a primary pituitary myxoedema, started normal menstruation after 2 months' treatment with thyroid.

It is concluded that completely normal adrenal and pituitary function is present only in primary myxoedema of recent onset, and that the disturbances of function that occur as the condition progresses tend to become irreversible with time.

Peter C. Williams

2033. **A Study of a Family of Goitrous Cretins**

J. B. STANBURY and A. N. HEDGE. *Journal of Clinical Endocrinology* [J. clin. Endocrinol.] 10, 1471–1484, Nov., 1950. 9 figs., 7 refs.

A married couple with no sign of thyroid abnormality and living near the sea-coast had 3 normal children and then 4 goitrous cretins. Three of the cretins and one of the normal children are described.

Thyroidectomy was performed on 2 of the cretins; the gland removed consisted of areas of hyperplastic tissue amidst involuted, atrophic, or fibrotic tissue. The blood protein-bound iodine level was 1 μ g. per 100 ml. or less in the cretins; when they were given radioactive iodine it was accumulated in the thyroid abnormally fast, but the further processes of thyroxine synthesis were absent, as shown by the rapid discharge of the accumulated iodine when potassium thiocyanate was given 24 hours later. The normal sibling accumulated radioactive iodine in the thyroid at the normal rate and there was no discharge of it when thiocyanate was administered.

Peter C. Williams

2034. **An Interpretation of the Goitrogenic Properties of Certain "Antithyroid" Agents**

F. X. GASSNER, M. L. HOPWOOD, E. A. HERROLD, and A. J. PLUMMER. *Journal of Clinical Endocrinology* [J. clin. Endocrinol.] 10, 1485–1493, Nov., 1950. 8 figs., 11 refs.

As high concentrations of iodide are known to inhibit the action of thyrotrophin, it is possible that an iodinated antithyroid drug might inhibit thyroxine synthesis, yet by virtue of its iodine content also inhibit thyrotrophic activity and so be unaccompanied by goitrogenic properties. An iodinated compound might also be accumulated more readily in the thyroid gland.

Some evidence in confirmation of this view has been obtained by preliminary experiments with 5-iodothiouracil and with 2-carboxymethyl-5-iodo-6-propylthiouracil. These compounds have antithyroid activity comparable with that of the non-iodinated compounds, as shown by their capacity to depress oxygen consumption in guinea-pigs and prevent the uptake of radioactive iodine by the chick thyroid; they also reduce the iodine content of the chick thyroid.

When the non-iodinated compounds are given to chicks injected with thyrotrophin the increase in thyroid

weight is greater than the sum of the increases produced by the antithyroid drug and by thyrotrophin given alone: with the iodo-compounds the increase is no greater or, particularly with iodopropylthiouracil, is less than the sum of the separate increases. This result is unaffected if potassium iodide is given with the non-iodinated compounds in doses containing equivalent amounts of iodine to those in the iodo-compounds. When the iodo-compounds are given alone in doses equivalent to those which, with the non-iodinated compounds (alone or with potassium iodide), produce an increase in thyroid weight and hyperplasia, then the thyroid weight is increased only by follicular enlargement, and no hyperplasia results.

It is concluded that thiouracil reinforces the action of thyrotrophin in some way, whereas iodothiouracil antagonizes it.

Peter C. Williams

ADRENAL GLANDS

2035. Use of Adrenolytic Drug, Regitine, in Pheochromocytoma

L. T. ISERI, H. W. HENDERSON, and J. W. DERR. *American Heart Journal* [Amer. Heart J.] 42, 129-136, July, 1951. 6 figs., 13 refs.

Administration of "regitine", an adrenolytic drug, in doses of 25 mg. by mouth every 3 hours controlled the blood pressure before and during the removal of a pheochromocytoma from a boy of 8 years. It was also effective by the intramuscular and intravenous routes.

D. Verel

2036. Diminished Adrenal Cortical Function in Diabetes as Shown in Eosinophil Response to Stress of Surgery

J. B. FIELD and A. MARBLE. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 77, 195-198, June, 1951. 3 figs., 8 refs.

Recent observations have suggested that in diabetes there is a reduction in adrenal cortical function, shown by subnormal excretion of 17-ketosteroids. The present paper reports a study made in Boston on the eosinophil response of diabetics undergoing major surgery, adrenal cortical activity being, in general, reflected by the level of circulating eosinophils. The technique described by Hills *et al.* (*Blood*, 1948, 3, 755) was used for eosinophil measurement. Counts were made on the pre-operative day and the second post-operative day in 25 diabetic and 13 non-diabetic patients undergoing major operations which were, so far as possible, of the same type in both series.

All the non-diabetic patients showed a fall in eosinophil count by more than 50% after operation—a response which is accepted as normal; whereas in 10 of the 25 diabetics the depression was less than 50% of the pre-operative level—a significant deviation from normal. Of the diabetics 5 failed to show a normal fall in eosinophil count after receiving ACTH—a further indication of adrenal insufficiency; normal response to administration of adrenal cortical hormones (given as "cortone") showed that the eosinophils themselves were sensitive to stimulation.

In the cases studied there was some correlation between diminished adrenal activity and duration of the diabetes. The authors suggest that the adrenal insufficiency may be a compensatory change counterbalancing insulin deficiency. There was no indication that the adrenal changes had resulted from malnutrition, as has been suggested previously.

Nancy Gough

2037. Treatment of Congenital Adrenal Hyperplasia with Cortisone

L. WILKINS, R. A. LEWIS, R. KLEIN, L. I. GARDNER, J. F. CRIGLER, E. ROSEMBERG, and C. J. MIGEON. *Journal of Clinical Endocrinology* [J. clin. Endocrinol.] 11, 1-25, Jan., 1951. 8 figs., 18 refs.

Congenital adrenal hyperplasia differs from Cushing's disease in having symptoms chiefly attributable to excess androgen secretion rather than to excess corticosteroid; these are accelerated growth, muscular development, and epiphyseal ossification, early growth of sexual hair, and progressive virilization. The condition causes pseudohermaphroditism in females and macrogenitosomia praecox in males. There is little sign of disturbed electrolyte or carbohydrate regulation in most cases, though in some electrolyte imbalance causes Addisonian symptoms and sometimes death. Attempts to suppress androgen secretion or, perhaps, to antagonize its peripheral actions by the injection of compounds with similar structure and little androgenic activity have failed. Treatment with cortisone has, however, given good results. Since cortisone reduces the adrenal weight of intact rats but not of hypophysectomized rats maintained on a constant dosage of adrenocorticotrophin, it presumably suppresses secretion of the latter.

The present paper records the results of such treatment in 10 cases: a 2-month-old girl, 5 female pseudohermaphrodites aged 8½ to 18½, 2 boys aged 2 and 2½ years with macrogenitosomia praecox, and 2 infants treated elsewhere. The older patients were given 50 to 100 mg. of cortisone acetate daily, and the younger ones 25 to 50 mg. In all cases the excretion of 17-ketosteroids and of oestroids (oestrogens determined fluorimetrically) was reduced during treatment: 17-ketosteroid excretion values averaged 3.5 to 53 mg. per day before treatment and 0.3 to 7.1 mg. daily during treatment; the corresponding figures for oestroids were 23 to 105 µg. and 8 to 40 µg. daily. When cortisone injections were stopped the excretion rates, after several days' delay, reverted towards the pre-treatment levels. Treatment was continued for 3 to 5 months in some of the children and there was no sign of refractoriness. Bioassay of the urinary androgens in 2 cases and of the oestrogens in 1 case showed that these were reduced to a greater extent than the corresponding 17-ketosteroids and oestroids. Apparently metabolites of cortisone contribute towards the total 17-ketosteroids estimated, and this may account for the failure to reduce the excretion rate to values below 3 to 6 mg. per day in the older pre-adolescent children, who failed to show androgenic effects despite such adolescent levels of excretion.

The urinary corticosteroids were also excreted at rates above normal before treatment. The changes during

treatment were irregular, probably because diminished secretion by the adrenal may be masked by excretion of some of the administered cortisone.

The response of one patient to 100 mg. of adrenocorticotrophin was tested. There was no increase in urinary excretion of 17-ketosteroids, corticosteroids, or oestroids before treatment, possibly because the adrenal was already secreting at its highest rate. There was some increase during treatment with 25 mg. of cortisone daily and none when this dosage was doubled. The possibility of the development of adrenal resistance to trophic stimulation is discussed. In one patient with severe Addisonian electrolyte disturbance which could not be adequately controlled with a high sodium chloride intake normal, though fluctuating, blood chemistry was restored when cortisone was given. In cases where the electrolyte disturbance was controlled by deoxycortone, cortisone had little or no effect in this respect. Of 2 patients who had hypertension, blood pressure was restored to normal in one, but in the other excitability, which developed during treatment, exacerbated the hypertension so that treatment had to be stopped.

Most of the patients have not been treated long enough to assess the effects on virilization, but there has been abolition of clitoris erection in 1 case and decrease of acne and seborrhoea in 3 cases. There has also been some definite feminization: development of the breast and oestrogenic changes in vaginal cytology have occurred in 2 cases, in one of which menstruation was initiated. It is suggested that treatment releases gonadotrophin secretory function previously inhibited by the excess androgen.

Peter C. Williams

2038. **Joint Affections after Treatment of Adrenal Deficiency with Deoxycortone Acetate.** (Поражение суставов при лечении больных с недостаточностью надпочечников дезоксинокортикостерон-ацетатом) V. G. BARANOV and A. D. SUKHODAROVA. Клиническая медицина [Klin. Med., Mosk.] 29, No. 7, 22-24, 1951.

Adrenal steroids may be classified under three headings: (1) those regulating electrolytes; (2) those regulating carbohydrate metabolism; and (3) those having an action similar to that of the sex hormones. In this paper are reported 4 cases of adrenal deficiency treated with deoxycortone acetate (DCA) in which joint pains and periarticular changes developed and which disappeared on withdrawal of the drug. The authors correlate this observation with Selye's experiments with DCA on rats, in which severe joint changes and even the development of granulation tissue in the joint cavities were found after the administration of mineralo-corticoids. They recommend reduction of the dose of DCA to a minimum in cases presenting these symptoms, with administration of a diet poor in potassium and containing abundant sodium chloride.

[While these conclusions are, as is pointed out by the editor of the journal in which the paper appears, based on insufficient data, they are worthy of further investigations on a larger scale, and, if found valid, may necessitate the administration of glucocorticoids in cases of

Addison's disease in which joint affections develop after treatment with DCA.]

L. Firman-Edwards

PITUITARY GLAND

2039. **Acromegaly and the Heart: a Clinical and Pathologic Study**

M. R. HEJTMANCIK, J. Y. BRADFIELD, and G. R. HERRMANN. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 1445-1456, June, 1951. 4 figs., 18 refs.

The heart has been studied in 21 classic cases of acromegaly. In 13 of the patients there was clinical evidence of heart disease, and 5 were admitted to hospital in frank congestive heart failure. The duration of acromegalic symptoms could not be correlated with the incidence of heart disease. Electrocardiograms were available in 15 cases, in 6 of which there was impaired intraventricular conduction; in 2 there was complete left bundle-branch block and in 4 incomplete branch block. Six patients had hypertension. Necropsy was performed in 4 cases and hypertrophy of myocardial fibres was found in all of them. Some interstitial fibrous-tissue proliferation was present in 2 cases. Hypertension is unusual in acromegalics, but when it occurs they tolerate it badly. The heart in 1 of these 4 cases weighed 1,140 g.

C. L. Cope

2040. **Hormonal Treatment of Simmonds's Disease**

J. D. ROBERTSON and H. F. W. KIRKPATRICK. *Lancet* [Lancet] 2, 54-57, July 14, 1951. 3 figs., 34 refs.

A 47-year-old man with Simmonds's disease caused by trauma involving the pituitary gland was studied for a period of some 4 months. During different periods of time he was given ACTH in doses up to 100 mg. daily, cortisone 100 mg. daily, and a combination of deoxycortone acetate and testosterone by implantation, with thyroid extract by mouth. Over the whole period of observation there was great improvement in general health with a gain of 23½ lb. (10.65 kg.) in weight. The blood pressure rose from 100/65 to 145/90 mm. Hg and the basal metabolic rate from -40 to -13%. The rate of improvement was not obviously better during any one of the three periods of treatment. Studies of electrolyte levels in urine and serum and of urinary output of 17-ketosteroids and corticosteroids did not yield any new information, and the carbohydrate tolerance was not significantly altered.

A. C. Crooke

2041. **Disorders of Regulation of Water Metabolism in Diseases of the Pituitary and Diencephalon.** (Fehlregulationen im Wasserhaushalt bei Erkrankungen des Hypophysen-Zwischenhirnsystems)

H. LEVERINGHAUS. *Zeitschrift für Klinische Medizin* [Z. klin. Med.] 148, 12-24, 1951. 2 figs., 23 refs.

This is a brief summary of the function of the pituitary and hypophysial structures in connexion with water metabolism. Information is presented to show the action of these structures upon the function of the kidney tubules, with comments on the delay of cause and effect, and details of clinical application with special reference to surgical prognosis.

G. F. Walker

Dermatology

2042. **Dyshidrosiform Dermatitis of Hands and Feet Caused by an Aspergillus.** (Dermatite dyshidrosiforme des mains et des pieds, causée par un aspergillus)

X. VILANOVA and M. CASANOVAS. *Annales de Dermatologie et de Syphiligraphie* [Ann. Derm. Syph., Paris] 78, 292-296, May-June, 1951. 2 figs.

In the authors' patients dyshidrosiform dermatitis began on the feet; later it affected hands. The cause was found to be an aspergillus pathogenic to the guinea-pig and related to *Aspergillus ustus*. Local treatment was ineffective; permanent cure followed the administration of potassium iodide, 4 g. daily by mouth.

James Marshall

2043. **Treatment of Seborrheic Dermatitis with a Shampoo Containing Selenium Disulfide**

W. N. SLINGER and D. M. HUBBARD. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] 64, 41-48, July, 1951. 10 refs.

A shampoo containing 2.5% selenium disulphide was used in 90 cases of seborrheic dermatitis of all degrees of severity, and completely controlled the condition in 81 of the cases. Treatment consisted of two shampoos weekly for two weeks and one shampoo weekly thereafter. The best results were obtained in cases of common dandruff. In most cases itching and burning were soon relieved. The shampoo was also found useful for reducing scaling in other scalp conditions, such as atopic dermatitis. There was no evidence of systemic intoxication, local irritation, or sensitization in any of the cases, and patch tests with selenium disulphide produced neither primary irritation nor sensitization in 100 normal subjects.

E. W. Prosser Thomas

See also Hygiene and Public Health, Abstract 1749.

2044. **Bacitracin in Dermatology: its Effectiveness in Topical Therapy**

E. F. FINNERTY. *New England Journal of Medicine* [New Engl. J. Med.] 245, 14-17, July 5, 1951. 6 refs.

The author reports significant improvement obtained after the topical application of bacitracin in 83 cases: 75 of superficial pyoderma, 4 of secondary infection associated with varicose and traumatic ulcers, 1 of ischio-rectal abscess, 1 of recurrent boils, 1 of ulcer of the buttock, and 1 secondary scalp infection associated with psoriasis. The response of hitherto strongly resistant pathogenic infections was impressive. The use of bacitracin materially reduced treatment time and, since the incidence of allergic reactions is low, it is an excellent agent for the administration of topical therapy—probably the most effective now available.

During this investigation, bacitracin became the dressing of choice after all minor electrosurgery and

operative procedures for moles, skin cancers, and warts. The preparations used and their effects on various organisms *in vitro* and *in vivo* are described.

G. B. Mitchell-Heggs

2045. **Epilepsy in Systemic Lupus Erythematosus. Effect of Cortisone and ACTH**

P. W. RUSSELL, J. R. HASERICK, and E. M. ZUCKER. *Archives of Internal Medicine* [Arch. intern. Med.] 88, 78-92, July, 1951. 6 figs., 27 refs.

Previous work on the association of convulsions with lupus erythematosus has led to the view that the occurrence of epilepsy with rheumatoid arthritis may often indicate the existence of systemic lupus erythematosus. Convulsions were noted in 22 of 144 cases of lupus erythematosus described in the literature, the seizures being terminal in 15, and in 7 of the authors' series of 28 consecutive patients with a positive reaction to the plasma L.E. test. In 2 of these 7 the convulsions preceded the development of typical symptoms by 2 and 16 years respectively. In 3 further cases without convulsions there was evidence of cerebral dysrhythmia or histopathological changes. The incidence of convulsions bore some relation to disease activity, their occurrence in some cases being associated with exacerbation. Cortisone or ACTH diminished or abolished the convulsions in some cases; "dilantin" (phenytoinum sodium), which was given to 5 patients, was without effect.

Abnormal patterns in the electroencephalogram (EEG) were observed in 7 of 11 consecutive patients with active lupus erythematosus, including all the 5 patients with convulsions and 2 of 6 in whom there were no convulsions or other cerebral manifestations. Two types of electrical change were noted, the common feature being a slow, diffuse delta activity unequal on the two sides, contrasting with the symmetrical slow, diffuse waves found in idiopathic convulsive conditions. The degree of EEG abnormality tended to fluctuate with the clinical state.

The histological changes seen in the brain varied considerably and none could be regarded as specific.

R. Crawford

2046. **Is Psoriasis a Psychodermatosis? (Le psoriasis est-il une psycho-dermatose?)**

M. BOLGERT, R. POISSON, and M. SOULÉ. *Annales de Dermatologie et de Syphiligraphie* [Ann. Derm. Syph., Paris] 78, 273-291, May-June, 1951. 10 refs.

A review is given of the literature on psoriasis as a psychosomatic disease, with a description of 33 cases in which psychiatric investigations were made. Emotional trauma was positively related to onset of attack in 20 cases, probably related in 6, and apparently unrelated in 7. The authors found the nature of the trauma to be very variable.

James Marshall

2047. Prognosis of Dermatitis Herpetiformis Treated and Untreated

W. H. EYSTER and R. R. KIERLAND. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] **64**, 1-8, July, 1951. 2 figs., 4 refs.

This paper is based on the follow-up records of 381 patients diagnosed as suffering from dermatitis herpetiformis at the Mayo Clinic during a 20-year period ending in 1939.

The incidence of the disease was 1 in 500 skin cases, with a ratio of 2.7 males to 1 female. The age at onset ranged from 6 months (2 male infants) to 78 years, but in most cases the disease started in early adult life. The natural course of the disease was towards amelioration or complete remission after about 10 years. In one-quarter of the patients symptoms were worse during the summer. Almost all the patients were examined for foci of infection, but rarely did treatment or removal of these have any good effect. On the contrary, 5 patients said that their eruption began after tonsillectomy or extraction of teeth. The only aetiological factor which was consistent enough to be noted was a psychogenic component, which was present in about a third of the patients. Some of these, apart from exacerbations in association with nervousness, fatigue, overwork, or emotional upset of various kinds, suffered from hysterical dysphagia, psychoneurosis, cardiac neurosis, irritable bowel syndrome, anxiety state, or constitutional inferiority.

Eosinophilia was the most consistent blood change, but a count of more than 10% was unusual. Sensitivity to iodides and bromides was found in a large proportion of those tested, but was not constant enough to be of diagnostic value.

It was strikingly apparent that until the advent of the sulphonamides, and particularly sulphapyridine, no treatment, with the exception of arsenic, was of permanent value in controlling the disease. Most of the patients who improved temporarily did so in hospital, where rest was the main treatment. Arsenic had been used in 218 of the cases, and 47 of these patients developed keratosis, pigmentation, or other signs of arsenical poisoning. Of 130 patients given Fowler's solution 43 showed signs of chronic arsenical intoxication, but in only 5 of the 81 patients receiving Asiatic pills were there arsenical sequelae.

E. W. Prosser Thomas

2048. Some Observations on the Diagnosis of Clinically Pigmented Skin Tumours

M. R. EWING and T. POWELL. *British Journal of Surgery* [Brit. J. Surg.] **38**, 442-454, April, 1951. 15 figs., 20 refs.

Sclerosing angioma can mimic malignant melanoma sufficiently to deceive the most careful clinician, and even the pathologist may be misled by the naked-eye appearances or by a first glance at routine-stained sections. Two cases in which such mistakes led to more or less serious consequences stimulated the authors' study of the diagnostic problems presented by pigmented skin tumours in general.

They begin with a detailed description of 11 cases of sclerosing angioma. In addition, a series of cases of pigmented skin tumours was collected, and in these cases clinical diagnosis was found to be remarkably unreliable: of 28 diagnosed clinically as of malignant melanoma only 14 were confirmed pathologically; of 74 in which the diagnosis was benign melanoma (pigmented naevus) 34 were confirmed (2 being malignant); and of 12 cases in which the diagnosis was of pigmented papilloma only one was confirmed. Of 10 cases pathologically proved to be of sclerosing angioma and 3 of melanophoroma none was correctly diagnosed, and of 26 cases of pigmented papilloma only one. [The majority of the cases of pigmented papilloma were of the "verruca senilis" type. None of these mistakes is important except those where the diagnosis was of malignant melanoma.]

The authors believe that accurate clinical diagnosis of these cases is often impossible, and that the right course where there is doubt is local excision with an adequate margin, followed by radical measures only if necessary after a careful histological study which must include positive identification of the pigment concerned.

Bernard Lennox

2049. Treatment of Plantar Warts with Elastoplast and Podophyllin

D. A. DUTHIE and D. I. MCCALLUM. *British Medical Journal* [Brit. med. J.] **2**, 216-218, July 28, 1951. 6 refs.

The incidence of plantar warts appears to have increased in recent years. The authors believe expert radiotherapy to be the treatment of choice for the solitary plantar wart, but have investigated the results of treatment with "elastoplast" and podophyllin in a series of patients in whom radiotherapy was unsuitable or had failed.

If the wart has a horny surface, it is pared down as far as possible without causing bleeding. Elastoplast is then applied, starting on the dorsum of the foot and carrying it right round and overlapping. Two weeks later it is removed and any debris is gently scraped from the surface of the wart and the elastoplast reapplied. This procedure is repeated at intervals of two weeks, and if the wart does not come away at the second or third application treatment with podophyllin is started. A small quantity of a 25% suspension in liquid paraffin is rubbed in with a glass rod, any surplus dabbed off with wool, and elastoplast applied. The paring and application of podophyllin and elastoplast are then repeated at intervals of one to two weeks. The podophyllin is not effective unless it can be brought into contact with the filiform processes of the wart.

With this treatment 60% of cases were cured within two months, and 37 out of 40 within 18 weeks.

S. T. Anning

2050. Relapsing Panniculitis (Weber-Christian Disease). Review of Literature and Report of a Case including Treatment with Cortisone

C. R. SHUMAN. *Archives of Internal Medicine* [Arch. intern. Med.] **87**, 669-681, May, 1951. 2 figs., 47 refs.

Venereal Diseases

2051. The Problem of the Jarisch-Herxheimer Reaction in the Penicillin Therapy of Cardiovascular Syphilis

H. A. SINCLAIRE and B. WEBSTER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [Amer. J. Syph.] 35, 312-318, July, 1951. 20 refs.

The authors first review the literature on the treatment of cardiovascular syphilis with penicillin. Early investigators believed that penicillin was too dangerous an agent to be used in cardiovascular syphilis. Later studies with larger series of cases have shown that penicillin does cause severe Jarisch-Herxheimer reactions, but in 1949 most authors believed that penicillin should be used in the treatment of cardiovascular syphilis and that its use was without danger.

A series is described of 53 patients suffering from cardiovascular syphilis and treated with penicillin at the New York Hospital. Some patients were treated on an ambulatory basis. No patient suffered a therapeutic paradox. In the first group there were 9 patients with uncomplicated syphilitic aortitis. They were given penicillin in total dosage of 2 to 11.4 mega units; 6 had had previous heavy-metal therapy and 2 of them were receiving it up to the time of starting penicillin. In 2 of the 9 the temperature rose to 38.2° C. on the second day of treatment; one of these had previously been treated with heavy metals. Each of the 2 had neurosyphilis also. There were no untoward effects and both patients completed their treatment. The other 7 had no Jarisch-Herxheimer reaction and were completely asymptomatic during therapy. Two of these patients have since died, 1 a month after treatment from pulmonary embolism and the other 2 years after treatment from a non-cardiac disease. The remainder are still under observation.

In the second group there were 36 patients with aortic regurgitation who were treated with penicillin in total doses ranging from 3.3 to 12 mega units. Of these, 21 had received varying amounts of heavy metals before receiving penicillin; 6 had had heavy-metal therapy up to the time of starting penicillin. Of the total number 4, who also had neurosyphilis, had a rise in temperature as high as 38.4° C. during the first 48 hours of treatment, even though they had had heavy-metal treatment previously; these patients were asymptomatic throughout the rest of the course. Six patients died between 2 months and 3 years after completion of treatment: 4 died in cardiac failure and 2 from non-cardiac disease. The remainder are still under observation.

A group of 8 patients with aortitis and saccular aneurysm were treated with penicillin in a total dosage of 2.7 to 10.2 mega units. Seven had received previous heavy-metal therapy and 3 were receiving it until penicillin was started. There were no Jarisch-Herxheimer reactions or other untoward symptoms. All the patients are still under observation.

In the opinion of the authors penicillin is the method

of choice in the treatment of cardiovascular syphilis; the dangers of the therapeutic paradox and Jarisch-Herxheimer reactions do not appear to be significant.

H. S. Laird

2052. The Therapeutic and Toxic Effects of Penicillin in Syphilis. (La pénicilline, son action et ses accidents dans le traitement de la syphilis)

P. PHOTINOS. *Annales de Dermatologie et de Syphiligraphie* [Ann. Derm. Syph., Paris] 78, 297-299, May-June, 1951.

The rate of disappearance of treponemata from primary lesions is not related to the quantity of penicillin injected; single doses vary from 50,000 to 2,000,000 units. The author describes 3 cases in which there were grave toxic effects due to penicillin therapy: vesiculo-oedematous erythroderma, oedematous erythroderma with death from pulmonary oedema, and erythema multiforme with complete anuria lasting 36 hours.

James Marshall

2053. Congenital Syphilis in One of Apparently Identical Twins

R. A. RASKIN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [Amer. J. Syph.] 35, 334-339, July, 1951. 4 figs., 7 refs.

In this paper a case of congenital syphilis in one of apparently identical twins is presented. The twins were born at Beth Israel Hospital, New York. They were both male and were born on Aug. 4, 1949. It is not certain that the twins were identical, but evidence in favour of this being so is presented.

Twin A was diagnosed as suffering from congenital syphilis at the age of 9 weeks. The diagnosis was proved by blood and radiological examinations; the spinal-fluid Wassermann and colloidal-gold reactions were positive. Twin B was negative to all the tests. Twin A was given 3 mega units of penicillin in oil with 2% aluminium monostearate daily for 10 days and the other twin was given the benefit of the doubt and treated similarly. Both twins have been followed up for 8 months since October, 1949. Neither shows any signs of congenital syphilis, both are gaining weight and developing normally. All tests have been consistently negative in twin B. Twin A at 10 months has negative blood Wassermann, Kahn, and Mazzini reactions and the syphilitic changes are no longer apparent radiologically.

A number of theories about the pathogenesis of the condition are put forward.

H. S. Laird

2054. Some Observations on Neurosyphilis in the African Negro

R. R. WILLCOX. *Journal of Venereal Disease Information* [J. vener. Dis. Inform.] 32, 229-236, Sept., 1951. 19 refs.

Genito-urinary Disorders

2055. Semen Studies and Fertility

E. T. TYLER. *Journal of the American Medical Association* [J. Amer. med. Ass.] **146**, 307-314, May 16, 1951. 6 figs., 19 refs.

A sane and conservative evaluation is given of the male factor in 408 infertile marriages studied in Los Angeles. [The author's conclusions, while contributing nothing fresh, add confirmation to much of the work that has recently been done in this field.]

The standards used in the interpretation of seminal values are those adopted by the American Society for the Study of Sterility: a sperm count of 60,000,000 per ml., motility of 60%, and normal morphological forms in 75% are considered the minimum levels below which a specimen should be classified as infertile. [Most workers in Britain would consider these standards to be far too high and too rigid.] The author's findings confirm the fact that with a high sperm count the morphology and motility are in most instances found to be normal, and a constant relationship is demonstrated between the size of the sperm population and the eventual chances of conception. Little information concerning the aetiology of male subfertility was obtained beyond the observation that in many cases bilaterally small testes seemed to be associated with a poor-quality semen. The therapeutic effects of a variety of gonadotrophic and other endocrine preparations were tried and results were disappointing, although suggesting that there is possibly greater hope of success when some degree of selection of cases can be exercised rather than the empirical prescription of these drugs to all patients without discrimination.

[Though the author gives few details of his methods (for instance, he fails throughout to mention his definition of an infertile couple), these investigations have been thorough; comprehensive seminal study was made, on the average, more than six times on each patient. The paper is characterized by a healthy scepticism and common sense which should appeal to the reader.]

T. E. C. Barns

2056. Spermatogenic Rebound in the Human following the Administration of Testosterone Propionate

N. J. HECKEL. *Archives of Surgery* [Arch. Surg., Chicago] **63**, 4-8, July, 1951. 5 figs., 2 refs.

This paper from the Department of Urology (Rush) of the University of Illinois College of Medicine contains a report of investigations made on 18 out of a group of 49 physically normal men who were examined for sterility and found to have oligospermia, the total sperm counts varying between 5,000,000 and 60,000,000. Testicular biopsies revealed, in general, a disruption and disintegration of the normal sperm development, but not severe enough to be irreversible. Intramuscular administration of 150 mg. of testosterone propionate per

week in 3 doses of 50 mg. was continued until the sperm counts showed that a condition of severe oligospermia was present. The total dose given varied from 1,000 to 4,000 mg. Following the cessation of treatment the number of spermatozoa increased strikingly. Further biopsies at the height of the rebound showed an improvement in spermatogenesis, which in some instances became normal. [No explanation is given for this improvement in spermatogenesis.]

[As only one factor is considered in the sperm count the correlation between treatment and successful fertilization is also necessary.]

D. W. Higson

2057. The Effect of Cortisone on the Nephrotic Syndrome occurring in Diabetics

C. B. HOLMES, G. C. WALSH, M. M. BAIRD, D. M. WHITE-LAW, W. W. SIMPSON, and H. W. MCINTOSH. *Canadian Medical Association Journal* [Canad. med. Ass. J.] **65**, 26-29, July, 1951. 3 figs., 8 refs.

In this paper are described studies on 3 diabetic patients who had developed a nephrotic syndrome, and on the effect of cortisone on glucose tolerance, oedema, and serum and urinary protein content. The cortisone was given intramuscularly, 100 mg. daily for 37 days. In 2 of the patients the insulin dose was adjusted to control the level of fasting blood sugar and the degree of glycosuria; in the third patient the dose of insulin was maintained at a constant level.

Apart from the expected decrease in glucose tolerance on starting cortisone therapy, the results were, in general, inconclusive. No consistent effect was observed on the level of serum proteins, cholesterol, or non-protein nitrogen, or on haemoglobin, and no change in blood pressure or in ophthalmoscopic appearances was observed. In all 3 cases there was an increase in the total daily urinary protein excretion. Ketonuria was only once observed, and then in slight degree.

Clinically, in only one of the 3 patients was there any improvement in the nephrotic state: this was only temporary and was followed by a fatal relapse. In this patient the insulin requirement was found to decrease from the third week of treatment onwards, and possible reasons for this unexpected effect are discussed.

B. E. W. Mace

2058. Cation Exchange Resin in Treatment of the Nephrotic Syndrome

R. W. LIPPMAN. *Archives of Internal Medicine* [Arch. intern. Med.] **88**, 9-16, July, 1951. 2 figs., 10 refs.

The author describes the use of "Win 3000" (a cation exchange resin prepared in the ammonium cycle) in the treatment of nephrotic oedema in 14 patients whose ages ranged widely. The initial dose for adults was 32 g. daily, and this was increased as necessary to a maximum of 96 g. Children required a larger dose than could be

accounted for by difference in body weight. Pulverized resin, though possibly more effective than the granular form, was more difficult to prepare. The resin was given for periods of 5 days separated by rest periods of 2 days. The dose was decreased after the oedema had cleared up. Of the 14 patients, 11 had an excellent diuresis and most of them remained free from oedema subsequently during out-patient treatment. Two failures were due to inability to ingest the resin and the third failure was unexplained. The important hazards of treatment were severe acidosis and hypopotassaemia, and examples are cited in the case histories. Mild hypochromic microcytic anaemia was noted after long periods of continuous treatment. The underlying renal disease was not affected in any way by treatment with resin.

K. G. Lowe

2059. The Production of Urinary Casts during the Use of Cation Exchange Resins

I. S. FRIEDMAN, S. ZUCKERMAN, and T. D. COHN. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **221**, 672-677, June, 1951. 11 refs.

2060. Potassium Deficiency in Chronic Renal Disease

H. K. SCHOCH. *Archives of Internal Medicine* [Arch. intern. Med.] **88**, 20-27, July, 1951. 33 refs.

The author considers that subnormal plasma levels of potassium and clinical evidence of potassium deficiency are not uncommon in chronic renal disease, and cites 3 illustrative case histories. Decreased dietary intake, extrarenal losses (such as from vomiting), and relatively fixed urinary output of potassium are the factors responsible. The author presents details to show that the urinary loss of potassium is in excess of that amount filtered by the glomeruli, thus indicating continued tubular excretion, even in the presence of low plasma levels. The part played by the sodium-potassium ratio in the loss of fixed base is discussed. The chief features of the rather indefinite clinical picture are general weakness and muscular hypotonia, and electrocardiography gives little help in diagnosis. Prophylactic and therapeutic measures are briefly indicated.

K. G. Lowe

2061. Antihistamine Treatment of Acute Nephritis

D. LAWSON. *British Medical Journal* [Brit. med. J.] **1**, 1423-1425, June 23, 1951. 3 refs.

An account is given of an investigation into the use of antihistamine drugs in the treatment of acute nephritis. The well-known fact of the association of previous bacterial infection in acute nephritis and the possible part of immunity in the pathogenesis of the disease are discussed. Included in the series were 33 consecutive cases of acute nephritis, and alternate patients were treated with mepyramine maleate. All cases in the treated and control series were given penicillin for 5 days. Standard diet and fluids were also given and the same criteria for getting the patient up and about were observed.

The results are presented in tables and the following abnormal signs considered: oedema, hypertension, nitrogen retention, albuminuria, haematuria, and

raised erythrocyte sedimentation rate. The duration of each is noted separately, the longest of them being taken as the total duration of activity. The results showed a slightly slower return to normality in the mepyramine maleate series [in view of the total number in the series this is not statistically significant]. It is considered that there is no evidence that mepyramine maleate has any value in the short-term treatment of acute nephritis, although in this short series it was impossible to study the effect of the drug on the long-term prognosis.

P. G. Swann

2062. Anuria in Acute Nephritis

J. D. N. NABARRO and A. G. SPENCER. *British Medical Journal* [Brit. med. J.] **2**, 393-397, Aug. 18, 1951. 2 figs., 20 refs.

The authors report their observations on 2 women aged 45 years in both of whom acute nephritis developed after tonsillitis which had been treated with sulphonamides; anuria, preceded by oliguria for 4 to 5 days, not due to the sulphonamides, also developed. One patient, more seriously ill—blood urea level about 230 mg. per 100 ml., serum potassium concentration about 7.5 mEq. per litre, with general oedema, pulmonary oedema, and ascites—was treated with continuous peritoneal dialysis. The rinsing fluid had a pH of 8.4 and contained (in mEq. per litre): sodium 120, potassium 5, calcium 4, chloride 103, bicarbonate 26, with glucose 20 g., 10 mg. of heparin, and 10,000 units of penicillin per litre. With the flow of 45 litres in 4 days, 25 g. of urea was removed. The other patient, less seriously affected—blood urea concentration not exceeding 130 mg. per 100 ml., potassium level not above 6.7 mEq. per litre, no ascites or pulmonary oedema—was treated for 8 days with a gastric drip containing 400 g. of glucose and 100 g. of peanut oil in 1 litre of water every 24 hours. Both patients recovered.

It is argued that in the presence of marked metabolic disorder—as indicated by gross oedema, a serum potassium level approaching the fatal margin of 10 mEq. per litre, an abnormal potassium-nitrogen ratio in the serum, and acidosis—the use of peritoneal dialysis or the artificial kidney cannot be dispensed with, and the risks of these methods have to be accepted; otherwise a high-calorie diet with restricted protein, water, and electrolyte intake alone will be sufficient to bridge the patients over the dangerous period of 10 to 12 days of anuria.

L. H. Worth

2063. Type II Nephritis and Associated Diseases. [In English]

A. BERGSTRAND. *Acta Pathologica et Microbiologica Scandinavica* [Acta path. microbiol. scand.] **28**, 139-149, 1951. 9 figs., 23 refs.

2064. Treatment of Uremia by Perfusion of an Isolated Intestinal Loop. Survival for Forty-six Days after Removal of the Only Functioning Kidney

E. E. TWISS and W. J. KOLFF. *Journal of the American Medical Association* [J. Amer. med. Ass.] **146**, 1019-1022, July 14, 1951. 2 figs., 11 refs.

Disorders of the Locomotor and Osseous Systems

2065. Osteo-dental Dysplasia (Cleido-cranial Dysostosis). The "Arnold Head". [In English]

W. P. U. JACKSON. *Acta Medica Scandinavica* [*Acta med. scand.*] **139**, 292-307, 1951. 8 figs., 30 refs.

The finding of osteo-dental dysplasia in a 7-year-old Cape Malay boy who had been kicked by a horse led the author to trace the family back to its foundation by an immigrant Chinese who had 7 wives. He was able to find 356 descendants of this man, all resident in Cape Province; South Africa, 70 of whom were affected by the disease. Among the 31 members whom the author examined personally frontal bossing of the skull was a frequent finding, and in 6 cases the acromial ends of the clavicles were deficient; genu valgum was common. Dental manifestations included gross caries, accessory cusps, non-eruption of incisors, and cone-shaped teeth. Spina bifida was present in 3 cases. It is a remarkable fact that not a single affected member of this family over the age of 20 years has retained any teeth at all.

The literature of osteo-dental dysplasia is reviewed, some 500 cases having been recorded. In this peculiar condition an unknown causal agent seems to be at work from the 5th week of intra-uterine life, producing faulty enamel and dentine. The author considers "osteo-dental dysplasia" to be a more correct designation than "cleido-cranial dysostosis", and gives his reasons for this.

E. Neumark

2066. The Importance of Radiotherapy in the Treatment of Ankylosing Spondylitis

J. J. RICHMOND. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **44**, 443-447, June, 1951. 4 figs.

A review is given of 160 cases of ankylosing spondylitis treated by the author over a period of 7 years. The technique involved irradiation of the sacro-iliac joints and whole spine, irrespective of the stage of the disease. A skin dose of 2,000 r in 4 weeks was given to each section with x rays at 250 kV, 1 mm. Cu and 1 mm. Al filtration (H.V.L. 1.9 mm. Cu). This technique led to immediate symptomatic improvement of varying degree in 96% of cases and to freedom from recurrence of symptoms in 80%. [The latter figure includes cases treated 1 or more years previously, and cannot be regarded as a long-term result.] In the case of pre-menopausal females a tangential-field technique was used to minimize the x-ray dose to the ovaries. Although amenorrhoea may not result in these cases, the danger of unfavourable genetic changes in later generations as a result of irradiation received cannot be ignored. Radiation reactions during treatment included mild nausea and lethargy in most cases.

The erythrocyte sedimentation rates determined before and after treatment showed no significant difference.

Basil A. Stoll

2067 (a). Calcium Succinate with Aspirin in the Treatment of Rheumatic Disease—I. A Clinical Evaluation

H. H. TILLIS and H. S. CONNAMACHER. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **10**, 118-121, June, 1951.

It has been claimed that "dolcin", a mixture of calcium succinate and aspirin, is more effective than salicylate alone by virtue of the increase in tissue oxygenation brought about by the succinate. A controlled experiment was carried out to investigate these claims. Patients were given dolcin and then a control preparation which, while indistinguishable, contained only aspirin and no succinate. Twelve patients suffering from either rheumatoid arthritis or osteoarthritis were treated, first with dolcin and then with the control preparation. The authors conclude that while dolcin often "gave relief from pain, the relief was symptomatic only, and the patient was no better than when aspirin was given alone".

W. Tegner

2067 (b). Calcium Succinate with Aspirin in the Treatment of Rheumatic Disease—II. Calcium Succinate with Aspirin as an Anti-rheumatic Agent

D. C. CRAIN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **10**, 121-125, June, 1951.

In order to investigate the claims of the manufacturers of "dolcin" as an antirheumatic agent 2 groups of 4 patients suffering from rheumatoid arthritis were first treated with dolcin according to the manufacturers' instructions and later with an indistinguishable placebo containing only aspirin. It was hoped to keep the patients on treatment for 5 months, but only one patient taking dolcin and one taking the placebo would continue, the remainder saying they were receiving no benefit. Two groups of patients suffering from osteoarthritis were similarly investigated. The author concludes that while some patients reported subjective improvement, the result of this study showed that "dolcin is not an effective remedy for the treatment of rheumatoid or osteo-arthritis and has no advantage over aspirin alone".

W. Tegner

RHEUMATOID ARTHRITIS

2068. Total and Differential Protein Levels in the Blood and Cerebrospinal Fluid in Rheumatoid Arthritis

B. LUSH, M. F. CROWLEY, E. FLETCHER, and J. F. BUCHAN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **10**, 153-162, June, 1951. 17 refs.

After reviewing the literature on the protein level in blood and cerebrospinal fluid (C.S.F.) in rheumatoid arthritis the authors describe their findings in 23 cases of severe, chronically active rheumatoid arthritis. Their criteria for diagnosis, for chronicity (more than 4 years),

for activity, and for severity are defined. Cases with spinal involvement were not included. All lumbar punctures were done between L3 and L4, and nitrogen fractions were estimated by the micro-Kjeldahl technique. Serum fractionation was accomplished by sodium sulphite precipitation (42% w/v). Fibrinogen was not estimated. Total C.S.F. protein was estimated after 10% trichloroacetic acid precipitation, and fractionation was accomplished in half-saturated ammonium sulphate, with subsequent trichloroacetic acid precipitation.

Values for normal spinal fluids were obtained from the data of Izikowitz (1941), who used the same methods of analysis. It was found that the mean albumin concentration of the C.S.F. was significantly raised above normal limits in females (32.5 ± 3 mg. per 100 ml. fluid compared with the normal 24.8 ± 0.91 mg. per 100 ml.) as was that of globulin in males (11.82 ± 1.56 mg. per 100 ml. compared with 7.71 ± 6.3 in normal persons). The total protein content was outside normal limits (as given by Izikowitz) in 3 cases, in 2 of which it was 9.4 and 9.6 mg. per 100 ml.; 7 of 23 had abnormal globulin values, but it was not possible to correlate these findings with those obtained by clinical examination or with the source of the disease.

A series of 15 correlation coefficients between the 6 variables are given, of which 12 are listed as reaching significant levels. There was a close correlation between the serum and cerebrospinal-fluid protein levels (total, albumin, and globulin). The well-known increase in serum globulin was confirmed. This interesting increase in protein in the cerebrospinal fluid may be the result of undue permeability of the haemato-encephalic barrier.

E. G. L. Bywaters

2069. Prolonged Uninterrupted Cortisone Therapy in Rheumatoid Arthritis

E. W. BOLAND. *British Medical Journal* [Brit. med. J.] 2, 191-199, July 28, 1951. 30 refs.

The use of cortisone in the treatment of rheumatoid arthritis is beset with problems, including the withdrawal effects and relapse when the hormone is discontinued. For sustained improvement in a chronic disease such as rheumatoid arthritis it appears that cortisone must be given more or less continuously; but uninterrupted administration over long periods is liable to produce unpleasant, and sometimes dangerous, side-effects.

The author has treated 60 patients with rheumatoid arthritis with cortisone uninterruptedly for 6 to 15 months. Large suppressive doses were used, followed gradually by reduced dosage, and finally smaller maintenance doses. In this way adequate degrees of therapeutic control were maintained in a majority of cases. The ability to maintain satisfactory improvement varied indirectly, in general, with the severity of the rheumatoid arthritis. In 47% of severe cases very marked or marked anti-rheumatic response was maintained for long periods. This was so also in 70% of moderately severe cases and in 92% of moderate or mild cases. It was found that adverse hormonal side-effects often developed, and were the chief obstacles to better results in the more severe cases in which relatively large maintenance doses were

required to support satisfactory improvement. Unwanted side-effects developed also in 40% of all cases at some time during treatment, although most of these reactions were of a comparatively mild type and disappeared or lessened when the dosage of cortisone was reduced. It was unfortunate, however, that the lowering of dosage necessitated in such cases often, as would be expected, resulted in a clinical deterioration in the arthritis.

During prolonged cortisone therapy evidence of functional suppression of the adrenal cortex was present, as indicated by a decreased response of circulating eosinophils to exogenous ACTH. Such depression of function, however, was found to be of a temporary nature and in patients from whom cortisone was withdrawn after 6 to 14 months of continuous administration it was found that cortical function tests had returned to normal within periods ranging from 10 to 90 days.

The author points out that as experience with hormone therapy of this type expands, it becomes increasingly evident that there are distinct limitations, difficulties, and dangers in its long-term administration. In the present state of knowledge it appears that cortisone may be employed as a powerful weapon in the management of many cases of rheumatoid arthritis, but it should not be considered as the treatment of choice in most cases, and not as a cure in any case.

[This paper reports the largest and longest series of cases treated with cortisone to date; the author was a pioneer in its clinical development. It is therefore of great importance, and should be read by all clinical workers in this field.]

W. S. C. Copeman

2070. Changes in the Bone Marrow in Rheumatoid Arthritis; the Effect of Cortisone. (Über die Beteiligung des Knochenmarkes bei der Polyarthritiden chronica rheumatica und ihre Beeinflussung durch Cortison)

B. JASIŃSKI and A. STAECHELIN. *Schweizerische Medizinische Wochenschrift* [Schweiz. med. Wschr.] 81, 619-623, June 30, 1951. 13 refs.

During the last 10 years 80 patients with rheumatoid arthritis have been investigated, 6 of them having been treated by short courses of comparatively small doses of cortisone. Chronic granulocytopenia was present in 5 cases and in one of them an anaemia. Bone-marrow biopsy showed maturation arrest at the metamyelocyte and stab-cell stages; this was not influenced by cortisone. The functional activity of leucocytes was investigated by studying the disposal of bacterial substances, using a preparation made from *Bacterium coli*; this was diminished throughout. In 5 cases in which the leucopenia was not so severe, and in 5 with anaemia, bone-marrow changes were similar. In another case thrombocytopenia persisted for 2 months. Of the 4 patients without changes in the blood count 2 were given cortisone. In most cases the proportion of plasma cells in the marrow was less than 2%, but in 1 it was 3.4%. [This is much less than was found by Hayhoe and Robertson Smith, *J. clin. Path.*, 1951, 4, 47.] All the 16 cases in which there was evidence of bone-marrow

damage showed reactions to the injection of bacterial products similar to those seen in marrow hypoplasia or aplastic anaemia.

E. Neumark

2071. Joint Temperature Measurement in the Evaluation of Anti-arthritis Agents

J. L. HOLLANDER, E. K. STONER, E. M. BROWN, and P. DE MOOR. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 701-706, July, 1951. 6 figs., 8 refs.

The authors consider that criteria for judging improvement during drug treatment in rheumatoid arthritis are unsatisfactory. They record studies of the internal temperature of affected joints, suggesting that such measurements may prove more valuable. Previous work had shown that the internal temperature of a rheumatoid arthritic joint varies little from day to day under standard conditions, except when changes in the activity of the disease occur. To determine the temperature a filamentous copper-constantan thermocouple was inserted into the joint space through the bore of an aspirating needle, an electronic potentiometer automatically recording the temperature readings.

The effect of various anti-rheumatic agents was studied, usually in patients with an affected knee-joint. Throughout the observation period daily temperatures were recorded in 21 patients with active rheumatoid arthritis. Eleven of these received cortisone parenterally (300 mg. on the first day, then 100 mg. daily) and 10 patients received ACTH (80 mg. daily). In addition, cortisone acetate tablets were given orally to 6 patients with rheumatoid arthritis (150 mg. daily for 3 days, then 100 mg. daily) and a further 8 patients received various supposedly anti-arthritis agents.

In all the patients given ACTH or cortisone parenterally a fall in joint temperature within 24 hours was recorded, from a minimum of 0.7°C . to a maximum of 2.7°C . (mean 1.4°C .). During the pre-injection period there had been a maximum fluctuation of 0.4°C . Joint temperature continued to decrease, approaching normal levels in 3 to 5 days. The fall preceded detectable clinical improvement in 14 of the 21 patients, and in all but 2 preceded by some days any significant change in erythrocyte sedimentation rate. In all cases joint temperature began to rise within 24 to 48 hours of cessation of treatment; this rise preceded clinical relapse in 17 instances. In 14 patients joint temperature had returned to pre-treatment levels within 1 week of cessation of cortisone or ACTH therapy. In all 6 patients receiving cortisone orally a marked fall in joint temperature was noted within 48 hours. The steroids used in this investigation were 16-dehydropregnenolone acetate, 21-acetoxypregnenolone, Δ -5-pregnenolone, and testosterone propionate, and the 8 patients given one or other of these substances believed they were receiving cortisone. None of these agents produced any significant fall in joint temperature, nor was there any clinical improvement. In each case a prompt and marked fall occurred after cortisone.

The authors suggest that serial joint temperature determination might provide a rapid and relatively simple test of drug effectiveness in active rheumatoid

arthritis. By this criterion no other drug has been found to have an effect comparable to that of ACTH or cortisone; and it is shown that oral administration of cortisone is comparable in effectiveness with parenteral administration.

Kenneth Stone

2072. Involvement of the Hips in Rheumatoid Arthritis in Adults. (L'atteinte des hanches dans la polyarthrite chronique évolutive de l'adulte)

J. FORESTIER, J. ARLET, and F. JACQUELINE. *Revue du Rhumatisme* [Rev. Rhum.] 18, 304-309, June, 1951. 4 figs.

Involvement of the hip-joints in rheumatoid arthritis is not commonly seen, but the authors found the incidence to be at least 10%. A study of 40 such cases (32 women, 8 men) at Aix-les-Bains suggested that the disease, usually in a severe form, had at the time of investigation been present for a minimum period of 5 years. Four stages are described in the evolution of rheumatoid arthritis of the joint beginning, radiologically, with narrowing of the upper and inner part of the intra-articular space and ending with deformity of the femoral head and acetabulum, with displacement of both in an upward and inward direction. Arrest may take place at any stage, with development of bony sclerosis; bony ankylosis apparently never occurs.

The importance of early recognition is stressed, and one physical sign which may help to distinguish the condition from osteoarthritis is mentioned—flexion of the hip is limited at an early stage.

D. Preiskel

2073. Ulnar Deviation of the Fingers

G. R. FEARNLEY. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 10, 126-136, June, 1951. 6 figs.

The author points out that ulnar deviation of the fingers is certainly frequently found in rheumatoid arthritis, but it can also occur in such conditions as gout and Parkinson's disease. The commonly suggested causes of ulnar deviation are the effect of gravity and muscle imbalance. Gravity is probably not the sole cause of the deformity, for an ulnar deviation may affect one hand only although the arthritis affects both hands equally. The deformity is also not due to muscle imbalance, for on the whole the muscles of the fingers and hand tend to produce radial movement even in advanced wasting.

From studies of the normal hand it is concluded that if interphalangeal extension is maintained and the metacarpo-phalangeal joints are flexed, there is a tendency to ulnar deviation. In rheumatoid arthritis gripping entails just such an extension of the interphalangeal joints and flexion of the metacarpo-phalangeal joints, for the proximal interphalangeal joints in this condition tend to become stiff in extension, whereas the metacarpo-phalangeal joints become abnormally mobile, especially laterally. As the little finger shifts to the ulnar side it ceases to act as a bulwark and allows ulnar deviation of the remaining fingers.

Three stages of deviation are recognized, voluntarily correctible, passively correctible, and fixed ulnar. The little finger alone is sometimes affected.

W. Tegner

Neurology

2074. The Electroencephalogram in Cases of Subdural Hematoma and Hydroma

J. F. SULLIVAN, J. A. ABBOTT, and R. S. SCHWAB. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. and clin. Neurophysiol.] 3, 131-139, May, 1951. 5 figs., 22 refs.

Satisfactory electroencephalograms (EEG) were recorded from 32 patients with a subdural haematoma or hydroma, subsequently confirmed by operation and without evidence of an underlying brain lesion. In 23 cases the date of injury was known; it was during the week before the EEG was taken in 6 instances, but the average interval for the remainder was 10 weeks, so that the series is weighted in favour of chronic lesions.

Correct lateralization was achieved in 75% and localization in 47%, on the basis of 2 types of abnormality, occurring singly or together. Local slow-wave activity has been frequently described before, but the authors are more interested in local suppression of alpha rhythm; this they distinguish from the local suppression of all activity described by Jasper, Kershman, and Elvidge and long regarded as the classic response to subdural haemorrhage. It is pointed out that "monopolar" recording is unsuitable for demonstrating this asymmetry of alpha rhythm, and that close spacing (3 cm.) of electrodes may be necessary.

Of 28 unilateral lesions, 15 were associated with unilateral suppression of alpha rhythm. The authors consider that this EEG finding is sufficient to justify mention of subdural haemorrhage as a possible diagnosis. [It may reasonably be objected that there are many possible causes of such asymmetry, that the variations in the normal are considerable, and that the commonest causes of minor asymmetries are of a technical nature; nevertheless, there is no doubt of the usefulness of these observations, if handled with care.] W. A. Cobb

2075. The Aetiology of Partial Atrophy of the Thenar Eminence. (Zur Ätiologie der partiellen Daumenballentrophie)

W. GRONEMEYER. *Deutsche Medizinische Wochenschrift* [Dtsch. med. Wschr.] 76, 857-860, June 29, 1951. 10 figs., 43 refs.

The author draws attention to the relative frequency of "partial thenar atrophy" (Wartenberg) in clinical practice, and describes the clinical findings in 20 cases. The condition is due to wasting of the opponens and abductor brevis pollicis muscles. The natural history of the condition falls into 3 stages: (1) The neuralgic stage, in which there are transient pain and paraesthesiae in the shoulder, outer border of the arm and forearm, and in the first 3 digits. There is often intermittent stiff neck, with exacerbations of the symptoms by moving the neck. This stage is often misdiagnosed as "rheumatism". (2) In the second stage disturbances of sensation

appear, with hypalgesia and hypaesthesia in an area corresponding to the 6th and 7th cervical dermatomes on Keegan's scheme. In addition, there is often almost complete analgesia of an area overlying the lower third of the radius and including the thumb and the radial half of the index finger ("radial pain area"). This stage passes into (3) the pain-free third stage of radial thenar atrophy, where there is isolated wasting of the opponens and abductor brevis pollicis muscles, with accompanying weakness of fine movements of the thumb. There is loss of tone and often fasciculation in the affected muscles. In female patients there is frequently complaint of weakness in wringing out clothes.

In all his cases the author found clinical and radiological evidence of disease of the cervical spine: clinically, painful limitation of movements, particularly to the back and sideways, with exacerbation of the pain and paraesthesiae in the first 3 digits; radiologically, cervical spondylarthrosis attacking predominantly the 5th and 6th intervertebral spaces with narrowing of the intervertebral foramina between C5, 6 and 7 by osteophytic outgrowths around the neurocentral articulation of Luschka, and the conversion of the normal cervical lordosis into a kyphosis.

The author regards partial thenar atrophy as just one of the many manifestations of cervical spondylarthrosis. He uses his findings to suggest that the opponens and abductor brevis pollicis are unique among the small muscles of the hand in having their innervation solely from cervical roots 6 and 7. The pronator weakness found in 12 out of 20 of his patients indicates, he thinks, that the pronator teres muscle is similarly innervated. This view, he states, produces a much closer correspondence of innervation between myotome and dermatome in the upper limb, using Keegan's map. [Fuller details of this theory and its implications with regard to previous authors' explanations of partial thenar atrophy, such as carpal-tunnel compression of the median nerve, are given in the same author's paper in *Dtsch. Z. Nervenheilk.*, 1951, 165, 457.] J. B. Stanton

2076. Neuromuscular Disorders Amenable to Wheat Germ Oil Therapy

R. RABINOVITCH, W. C. GIBSON, and D. MCEACHERN. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 14, 95-100, May, 1951. 28 refs.

Since 1936 the authors have treated 107 patients, mostly suffering from neuromuscular disorders, with wheat-germ oil. In 93, suffering from progressive muscular atrophy, myasthenia gravis, disseminated sclerosis, and various other conditions, there was no response to treatment. Definite improvement, however, occurred in 3 cases of dermatomyositis, in 5 out of 25 cases of progressive muscular dystrophy, in 5 out of 7

cases of a condition which the authors call "menopausal muscular dystrophy" (see Abstract 2077), and in 2 cases of muscular atrophy of uncertain aetiology. They consider that the conditions responding to wheat-germ oil are the ones which also respond to adrenal corticoids, and suggest that wheat-germ oil and tocopherols might be "building blocks" for steroid hormones.

J. W. Aldren Turner

2077. The Clinical Features and Response to Cortisone of Menopausal Muscular Dystrophy

G. M. SHY and D. McEACHERN. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 14, 101-107, May, 1951. 5 figs., 9 refs.

The clinical features of a neuromuscular disorder which the authors call "menopausal muscular dystrophy" are described. They have studied 12 patients, of whom 11 were women during the climacteric period or after. There is progressive weakness of muscles of the hip and shoulder girdles with little visible wasting, but a "soft" consistency of the affected muscles on palpation. There may be impairment of tendon reflexes associated with involved muscles: there is no weakness of the facial or bulbar muscles and no sign of involvement of the central nervous system. Creatinuria is surprisingly small. Biopsy examination of affected muscles shows a histological picture similar to that in α -tocopherol-deficient animals, with degeneration of muscle fibres which are undergoing necrotic changes.

In some of these patients there was a good therapeutic response to wheat-germ oil orally, while 5 received cortisone with marked improvement in muscular power. When administration of cortisone was stopped the patients relapsed within a few days; these patients were accordingly given a maintenance dose of 100 to 150 mg. of cortisone every 2 days and apparently have remained well for a period of 6 months.

J. W. Aldren Turner

2078. Acetylcholine Sensitivity in Diseases of the Motor System with Special Regard to Myasthenia Gravis

L. ENGBÆK. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. and clin. Neurophysiol.] 3, 155-161, May, 1951. 1 fig., 13 refs.

After occlusion of the brachial artery by a pressure cuff acetylcholine hydrochloride in saline solution was injected into it and the pressure was then released. In normal subjects a brief motor response occurred, usually flexion of one or more fingers; it was followed by flushing and sweating of the palm. The threshold dose for this effect was 150 to 250 μ g. in 14 normal women and 100 to 350 μ g. in 19 normal men. The threshold in myasthenic patients was raised. In 13 out of 15 women it was more than 300 μ g., while in 2 out of 3 men it was over 500 μ g. Following intramuscular injection of neostigmine the threshold was reduced in 10 out of 14 cases. In patients with progressive muscular dystrophy a raised threshold was found, whereas it was lowered in amyotrophic lateral sclerosis and other denervating diseases, with the exception of 3 cases of poliomyelitis 2 to 4 years after the acute state. In 1 case of congenital myo-

tonia only 5 μ g. of acetylcholine caused vigorous and prolonged contraction.

The results are discussed in relation to the known physiology of muscle and to their diagnostic usefulness.

W. A. Cobb

2079. Benign Essential (Heredofamilial) Tremor

C. H. DAVIS and E. C. KUNKLE. *Archives of Internal Medicine* [Arch. intern. Med.] 87, 808-816, June, 1951. 2 figs., 5 refs.

The syndrome of benign essential tremor was observed in 14 patients. The condition is characterized by a more or less rhythmical tremor with a rate of 4 to 12 per second. The tremor is usually absent or minimal at rest, but present on voluntary increase in muscle tonus as in holding a limb in a definite position, or in active movement. It is aggravated by emotional tension, fatigue, or discomfort due to cold, and is relieved by repose or sedation. The hands, forearms, neck, head, and face are principally involved. There is no increase in tone, resistance to passive stretching, Kayser-Fleischer rings, nystagmus, or evidence of hepatic disease. On these grounds it may be distinguished from Parkinsonism and hepatolenticular degeneration, although most of the authors' cases had previously been diagnosed as of paralysis agitans. There are no defects in reflex responses or in sensation.

The condition may first become noticeable at any time from infancy to old age, but the commonest period is between 20 and 50 years. It often progresses at first for several years, and then may remain more or less unchanged for a long period, finally deteriorating rapidly in late adult life. Most of the patients described gave a clear history of one or more of their close relatives being affected with a similar disorder; 2 patients in the series came from the same family. Pedigrees of 6 of the families are given and the trait appears to be inherited as a simple Mendelian heterozygous character.

Scopolamine and allied drugs were found to have no significant value in treatment. Trihexyphenidyl therapy in 3 cases produced no noticeable response. Phenobarbitone often gave symptomatic relief, but the effect was probably largely non-specific.

Harry Harris

BRAIN

2080. Late Sequelae of *Haemophilus influenzae* Meningitis. (Seinfolger av *Hemophilus-influenzae*-meningitis) S. HESTETUN. *Nordisk Medicin* [Nord. Med.] 45, 965-968, June 20, 1951. 10 refs.

The mortality of patients suffering from *Haemophilus influenzae* meningitis has, in the experience of the author, now decreased to 10% compared with 90% to 100% before 1940. It has, however, been difficult to assess the after-effects, and for this purpose the Paediatric Department of Ullevål Hospital readmitted the patients who had suffered from this disease between 1940 and 1949. Of 32 patients, 19 were available for full examination; 11 had died before streptomycin became available, and the other 2 could not be examined for various reasons.

The average age of the patients when the meningitis was diagnosed was 2 years and 3 months. The re-examination was carried out after a lapse of time averaging 3 years and 10 months.

Prognosis depends largely on early diagnosis and consequent early admission to hospital. The number of cells found in the cerebrospinal fluid (C.S.F.) gave no indication of the prognosis, since in the cases quoted there was scarcely any difference between the number of lymphocytes in the C.S.F. of patients who died and those who survived. It was, however, found that the sugar content of the C.S.F. gave an indication of the severity of the disease. Treatment had varied according to therapeutic progress; some had received sulphonamides, others streptomycin, and yet others a combination of both.

Of 6 of the 19 patients who, at the peak of their illness, had suffered from convulsions or paresis, 3 were found to be completely free from any neurological symptoms, 2 showed slight changes in the electroencephalogram (EEG), and 1 retained a spastic hemiparesis. In 4 patients the vestibular function was abolished, but as Romberg's sign was negative other parts of the central nervous system appeared to have taken over this function. The hearing of 3 patients was more or less impaired; 8 showed pathological changes in the EEG. These changes varied from sluggish waves of 2 to 3 seconds frequency with maximum bitemporal amplitude to sluggish waves spreading to both hemispheres and marked abnormalities in the left hemisphere. Additionally, in the fronto-temporal region, epileptiform potentials of cortical origin were registered, pointing to a comparatively widespread lesion in this region. No mental change or retardation was detected in any of these patients; 1 child only, whose hearing was impaired, was late in learning to talk, and 1, who was suffering from severe neurological sequelae, did not stand up to the I.Q. test.

The author believes that the changes in the EEG might have been due rather to encephalopathy caused by the presence during sickness of bacteria or their toxins in the subarachnoid space than to encephalitis; the fact that these patients had been drowsy or comatose adds weight to this hypothesis. The damage to the vestibular and cochlear functions was attributable either to a secondary otitis media or to inflammatory reaction of the tissue surrounding these nerves. Damage due to streptomycin, however, could not be ruled out.

E. S. Fountain

2081. Cisternal Puncture in Tumours of the Posterior Cranial Fossa. (Цистернальные пункции при опухолях задней черепной ямки)
S. A. DOMAZON. Вопросы Нейрохирургии [Vop. Neurokhir] No. 1, 29-32, 1951.

It is not always possible for tumours of the brain to be located correctly from the neurological findings. In the author's experience many patients complaining of symptoms suggestive of localization of the growth in the posterior cranial fossa have supratentorial tumours; the correct diagnosis may be made with the help of cisternal

puncture. The fluid is scanty in the presence of growth in the posterior cranial fossa and is under low pressure. Supratentorial tumours should be expected if the fluid is under high pressure and in large quantity.

Cisternal puncture proved safe and never gave rise to complications in any of the author's cases.

Z. W. Skomoroch

2082. Behaviour Disturbances in Epileptic Children

C. BRADLEY. *Journal of the American Medical Association* [J. Amer. med. Ass.] 146, 436-441, June 2, 1951. 33 refs.

Epilepsy is not a disease entity, but a symptom of disordered function of the central nervous system. In children the term epilepsy is used to include convulsive disorders or psychomotor attacks as well as "grand mal" and "petit mal". The behaviour disturbances are of two kinds. The primary disturbances are commonly found among epileptics and appear to be directly associated with the condition. Five of these behaviour traits are listed: (1) erratic variability in mood or behaviour, where the child has apparently purposeless fluctuations in social adaptability; (2) hypermotility, or restless overactivity; (3) irritability, or the tendency to become aggressive; (4) a short or vacillating attention span or an inability to concentrate; and (5) a selective difficulty in mathematics. The secondary behaviour traits are those resulting from the individual environment and are of no set type.

Modern therapeutics have made it possible to control the convulsions to a large extent, but the author emphasizes that behaviour traits, if present, are of equal or even greater importance in children. Phenobarbitone often exaggerates the difficulties, whereas diphenylhydantoin and, particularly, amphetamine often help greatly. The importance of careful individual approach and of psychological treatment for secondary traits is pointed out. Co-operation with those who have responsibility in rearing the child is essential.

E. H. Johnson

2083. Subacute Cortical Cerebellar Degeneration and its Relation to Carcinoma

W. R. BRAIN, P. M. DANIEL, and J. G. GREENFIELD. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 14, 59-75, May, 1951. 12 figs., 33 refs.

Subacute cortical cerebellar degeneration has been found in association with carcinoma in several cases; 4 further cases are reported. The apparent rarity may be due to symptoms having been attributed to metastases.

A woman of 61 became weak and ill, with unpleasant dreams and unsteady gait. Vision became blurred and there was difficulty in speech and diction. She had headaches and cramps in the legs. When admitted 2 months later she showed dysarthria and aphasia; vision was good, with no papilloedema, but there was nystagmus, with ataxia and unsteadiness. The cerebrospinal fluid (C.S.F.) contained increased cells and protein, the Lange curve was paretic, and the Wassermann reaction negative. Her condition deteriorated and

she died 3½ months from the onset. Necropsy revealed in one ovary 2 small masses of carcinoma. The cord showed early degeneration of the pyramidal tracts and direct spino-cerebellar and dorsal paths. The cerebellum revealed marked loss of Purkinje cells, with sudanophil extracellular lipid. There were fat-containing cells in the white matter and molecular layers. Some neuroglial increase was noted but no bushwork. There was perivascular cuffing in the cord and occasional glial stars.

A man of 48 became erratic at lawn tennis; 3 months later his gait was unsteady and he drove his car badly. Mental deterioration and loss of memory followed, and he experienced double vision, giddy attacks, and noises in the head. Six weeks later he had dysarthria and weakness of the external rectus. His arms were hypotonic with fine tremor and there was intention tremor and ataxic gait. The C.S.F. was normal. There was increasing dementia and drowsiness till death 7 months from the onset. Histological examination of the brain showed degeneration only in the cerebellum, especially vermis, with marked lipid deposits, especially in the molecular layer, and slight loss of Purkinje cells and baskets. There was diffuse gliosis of the molecular layers.

A woman of 54, after frontal sinusitis, felt tired and became weak; her mind "seemed to wander". Two months later there was dysarthria, mental instability, nystagmus, and weakness of limbs. The C.S.F. pressure and protein and cell content were increased. There were signs of carcinoma of the lungs. The patient died after 3½ months of illness. At necropsy oat-cell carcinoma of lungs was found, with no secondaries in the brain. The cerebellar cortex showed loss of Purkinje cells with preservation of basket cells, and loss of granule cells. There was lipid degeneration in the granule layer and white matter, glial stars, and cuffing of vessels in the cerebellum and medulla. Some lipid changes in the spino-cerebellar and dorsal tracts were observed.

A man of 56 had a vague illness from which he seemed to recover. Later he began to feel tired, became unsteady in his gait, had pains in back and legs, and felt giddy. Three months later there were diplopia, papilloedema and nystagmus. The arms were hypotonic with some intention tremor; his gait was ataxic. The C.S.F. pressure, cells, and protein were increased. A sub-tentorial decompression was performed but this was followed by haemorrhage, and death after 3½ months' illness. Necropsy showed an oat-cell carcinoma of the lung with secondaries in the adrenal glands. In the cerebellum there was increase in neuroglia with some bushwork; the Purkinje cells were lost in some areas, and granule cells were decreased. There was very little lipid change. The cervical cord showed some glial stars and cuffing, with early myelin changes in dorsal columns.

In all cases there was rapid development of cerebellar symptoms, with diplopia and some mental deterioration. In the cases associated with carcinoma the C.S.F. showed changes. In 11 of 16 cases reported there was carcinoma. The histology, showing evidence of katabolism of myelin, suggests that the Purkinje cells are especially vulnerable to poisons or intrinsic metabolic disturbances. The

perivascular cuffing is probably a reaction to rapidly degenerating nerve tissue. The chronic forms of cerebellar degeneration are not associated with carcinoma.

Gwenvron M. Griffiths

2084. Psychiatric Symptoms and Syndromes in Parkinson's Disease

R. S. SCHWAB, H. D. FABING, and J. S. PRICHARD. *American Journal of Psychiatry* [Amer. J. Psychiat.] 107, 901-907, June, 1951. 11 refs.

The purpose of this paper is to draw attention to some paroxysmal symptoms in paralysis agitans. After referring to the well-known variation of rigidity with the emotions, the possibility of intercurrent psychiatric illness, the occurrence of illness as a reaction to the disability itself, and confusional states due to the drugs used in medication, the authors describe a series of bizarre and interesting psychiatric symptoms. These symptoms are mostly associated with oculogyric crises, and include: (1) Paroxysmal anxiety attacks, states of object terror different from the chronic anxiety of a neurosis. (2) Paroxysmal attacks of compulsive thinking, counting, or repetition of words. (3) Paroxysms of depression lasting up to an hour, followed by return to normal mood. One patient was treated successively by administration of large doses of amylobarbitone, by psychoanalysis, and by leucotomy; he ultimately committed suicide. (4) Paroxysmal paranoid attacks. In one remarkable case the patient's eyes turned to the left during the oculogyric crises, during which he would feel "resentful and fearful of the whole left half of his environment". (5) Attacks of strange sensations in the limbs, sometimes with the feeling that a foreign body was present in the limb. (6) Feelings of unreality. (7) States of sudden severe tension and agitation. (8) Fatigue states, such as paroxysmal feelings of fatigue, which prevented the patient from swallowing more than once or from chewing more than once or twice.

These disorders "are of special interest in that they often comprise *formes frustes* of psychoses and neuroses, and afford an opportunity for study of the neural correlates of many types of mental disorders."

Elliott Emanuel

2085. Influence of Benadryl upon Electromyographic Recordings in Parkinsonism

J. J. GITT, W. M. LANDAU, and M. H. CLARE. *Diseases of the Nervous System* [Dis. nerv. Syst.] 12, 117-121, April, 1951. 2 figs., 16 refs.

The authors have studied 13 selected cases of idiopathic, post-encephalitic, and arteriosclerotic Parkinsonism at the Washington University School of Medicine, St. Louis. Electromyographic (EMG) recordings were taken, using surface and needle electrodes, from biceps brachii, triceps, and brachio-radialis muscles before and after giving 30 mg. of diphenhydramine intravenously. Similar EMG and simultaneous electroencephalogram (EEG) recordings were taken from 2 normal control subjects before and after such an injection; in these 2 persons no significant change was noted in any record. In cases of Parkinsonism exhibiting tremor the

amplitude of the tremor, as shown by the EMG, was reduced by from 50 to 90%, but its rate and regularity were not altered. In patients with muscular rigidity evident clinically the EMG showed continuous "tonic" activity in the muscles at rest, and this too was reduced considerably after the injection. Subjective awareness of increased facility in fine movements was often noted.

The authors consider that the site of action of the drug is supraspinal and subcortical. *John N. Walton*

2086. An Evaluation of Artane and Tolserol in the Treatment of Spastic Disorders

A. S. EFFRON and W. M. SCHULTZ. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **221**, 561-566, May, 1951. 19 refs.

SPINAL CORD

2087. A Case of Hematomyelia and Meningeal Hemorrhage after Childbirth. (A propos d'un cas d'hématomyélie et hémorragie méningée après l'accouchement) F. THIÉBAUT and J. S. ATAIDE. *Paris Médical* [Paris méd.] **41**, 289-294, June 2-9, 1951. 4 figs., 16 refs.

The authors comment on the extreme rarity of onset of haematomyelia after childbirth and then record the case of a woman of 38, mother of 2 children, who, 6 hours after a delivery in which the midwife was said to have flexed the patient's neck very strongly, developed a complete paraplegia. The following day examination revealed a flaccid paraplegia with urinary retention, loss of pain, temperature, and vibration sense as far as the second lumbar spine, and with evidence of meningeal irritation. Lumbar puncture revealed a grossly blood-stained fluid. She began to improve 8 days after the onset, in that power began to return in the legs and superficial sensation returned, though bilateral extensor plantar responses developed. The improvement continued steadily and seems to have been completed by the end of 6 weeks.

On this clinical evidence the authors make a firm diagnosis of haematomyelia with subarachnoid haemorrhage and provide a [characteristically Gallic] discourse on the causation of haematomyelia in childbirth and abortion. Reviewing earlier speculations, they reject the idea of "effort" as a cause of the disturbance, mention without comment a "vegetative vasomotor reflex disturbance", and proceed to the unqualified acceptance of an embolic causation. The embolus may reach the cord by the arterio-pulmonary route or via the paravertebral venous connexions. A short [and rather irrelevant] account follows of a case of hemiplegia following abortion.

It is suggested that this supposed embolic precipitating cause is further aided by a supposed lowering of the vascular resistance in pregnancy. The final point made covers the occurrence of deafness in subarachnoid haemorrhage.

[The diagnosis of haematomyelia with subarachnoid haemorrhage is by no means absolutely certain in this case. It is possible that this patient had an angiomatous

malformation of the anterior spinal vessels which produced subarachnoid haemorrhage and an associated ischaemia of the anterior portion of the cord. In view of this doubt in the diagnosis, the lengthy speculation on the mechanism of haematomyelia seems scarcely justified.]

L. A. Liversedge

2088. Symptoms Arising above the Level of Medullary Compression. (I sintomi sopralesionali nelle compressioni midollari)

V. NERI and C. PAIS. *Rivista di Neurologia* [Riv. Neurol.] **21**, 137-156, March-April, 1951. 1 fig., 12 refs.

The authors do not consider that the symptoms which occasionally arise above the level of the lesion in spinal compression have received the attention they deserve. They analyse such symptoms in cases described in the literature and in 12 of their own cases controlled by operation, and endeavour to classify them on a basis of the probable causative mechanisms. Thus tumours in the upper dorsal and cervical cord may produce symptoms of a variable and fleeting nature above the lesion by increase in the cerebrospinal-fluid pressure from obstruction of its circulation and/or stasis in the meningeal veins. In the case of high cervical tumours, the effects of the raised pressure appear within the cranium, giving rise to such symptoms as vomiting, bradycardia, syncope, hiccup, cough and dyspnoea, dysphagia, epileptiform convulsions, nystagmus and giddiness, headache, and, rarely, papilloedema. Another cause of symptoms above the level of the lesion is arachnoiditis, possibly of "toxic" origin, causing rigidity of the spine which may extend above the site of the lesion and even become so generalized as to resemble meningitis. Rarely, a myelitis may arise above the site of compression on a basis of ischaemia, haemorrhage, and softening. Symptoms above the tumour may occur with an associated syringomyelia. In certain infiltrating tumours of the cord alterations of electrical excitability of muscles innervated from above the lesion and hyperaesthesia may appear. In 1 case of the authors' such symptoms extended for seven segments above the superior border of the area of anaesthesia below the lesion. In some cases of extramedullary tumour the superior pole may reach a higher level and give rise to symptoms and signs at this level which are separated by an area of normal sensation from the segments affected by the lower pole of the tumour, thus simulating multiple tumours. Compression of the sympathetic centres in the dorsal cord between C8 and D3 cause Horner's syndrome with disturbance of sweating, temperature, and pilomotor response in the area innervated by the cervical plexus, but Horner's syndrome may be preceded by irritative symptoms including mild exophthalmos and mydriasis. Lesions in the lower segments of the dorsal cord may cause autonomic disturbances in the upper limbs, especially along the ulnar border.

[Some of the conceptions regarding the mechanisms producing these symptoms above the level of cord compression may well be unfamiliar to British readers. All but three of the papers referred to were published before 1930.]

J. B. Stanton

Psychiatry

2089. **Heredity in Senile Dementia.** (Studio sulla ereditarietà della demenza senile)

G. PLUCHINO. *Cervello [Cervello]* 27, 293-307, July, 1951. 15 refs.

The author examined the case records of 302 patients suffering from senile dementia admitted to the Neuropsychiatric Hospital at Voghera. In 115 cases the family history was completely negative, in 59 there was a remote history of alcoholism, and in 48 there was a family history of mental disorder and alcoholism, the latter being also present in the patient's personal history, while the remaining 80 cases showed numerous types of mental illness in the family history. Schizophrenia was the commonest psychosis met with in ascendants, descendants, and collaterals.

A brief description is given of the clinical features of senile dementia and of the Mendelian laws of inheritance. A report is made of 5 female cases of senile dementia in which a hereditary transmission of the disease is clearly evident. Heredity was of a recessive character in 3 cases; in the others it could not be ascertained whether the parent, apparently sane, was a heterozygote or not. After remarking on the difficulties of obtaining accurate statistical data the author expresses the view that the tendency towards senile dementia is transmitted as a recessive character.

P. Cassar

2090. **Psychosis due to Streptomycin.** (Un caso di psicosi da streptomycin)

G. LEGGERI. *Rassegna di Neuropsichiatria [Rass. Neuropsichiat.]* 5, 98-106, March-April, 1951. 11 refs.

The author, after a short review of the various neurological complications of streptomycin therapy, reports a case of confusional psychosis due to this antibiotic. The patient was a woman, aged 29 years, who was receiving 1 g. streptomycin daily for pulmonary tuberculosis in a single injection. Half an hour after the third injection she became aware of a sensation of internal restlessness and started identifying persons and objects incorrectly. Successive injections made these symptoms worse and rendered her irritable and impulsive. Three hours after the seventh injection a state of excitement came on with a flow of talk, emotional instability, and impulsive behaviour that necessitated her admission to hospital. Horizontal nystagmus and dermatographism were present. Streptomycin was suspended and the following day she became negativistic, refused to talk and to eat, and soiled herself with urine and faeces. Five days later she was cooperative and clean, but she was still subject to changes of mood and was disoriented slightly in regard to place and time. She continued to improve and was discharged 17 days after admission. She has remained well since her discharge a year ago.

The author attributes the psychosis in this case to the patient's idiosyncrasy to streptomycin and to the fact

that the drug was administered in a single large daily dose instead of in divided doses. He found only one other case of streptomycin psychosis reported in the literature.

P. Cassar

2091. **Leucotomy in Psychosomatic Disorders**

W. SARGANT. *Lancet [Lancet]* 2, 87-91, July 21, 1951. 2 figs., 11 refs.

Tension states are often held responsible for the origin or perpetuation of psychosomatic disorders, and it is the theme of this paper that leucotomy may be employed to relieve tension and to effect improvement in physical symptoms. Examples are given of its use in cases of asthma and eczema, "rheumatic" pains, and cardiac neurosis. Symptoms such as tachycardia and emotional lability in patients with hypertension may be removed by leucotomy, though the blood pressure returns after operation to its former level. Anorexia and psychogenic vomiting may respond favourably, and leucotomy may indeed be a life-saving measure.

The conclusion is that leucotomy is of value in the treatment of some psychosomatic disorders, but extreme caution is necessary, the patients must be carefully chosen, and the operation modified to suit each case.

[Emotional tension is at the root of much physical disorder; to attempt its relief by leucotomy must surely be a last resort. The observations reported in this paper show that the operation may benefit some seriously ill people and perhaps save life, but it is at least possible that psychotherapy in skilled hands would have done the same.]

Desmond O'Neill

2092. **Life Situations, Emotions and the Course of Patients with Arterial Hypertension**

M. F. REISER, A. A. BRUST, and E. B. FERRIS. *Psychosomatic Medicine [Psychosom. Med.]* 13, 133-139, May-June, 1951. 4 figs., 10 refs.

The influence of emotionally charged situations on the course of hypertension was observed in 230 patients. These were divided into five groups as follows: Group I, 92 patients given physical examination only; Group II, 40 patients studied from the medical and psychiatric aspect over a few weeks; Group III, 30 patients examined by physicians with psychiatric awareness over a longer period; Group IV, 49 patients investigated fully from the psychiatric aspect; Group V, 19 patients investigated and treated intensively by psychiatrists.

An attempt was made to establish correlations between, on the one hand, the onset of hypertension (so far as this was known), the occurrence of symptoms, such as headache, weakness, and muscle pains, and the occurrence of complications, and on the other hand, life situations which had special emotional meaning for the patient. In all three categories the correlation rate was lowest in Group I and highest in Group V. In the latter

group significant correlations were found to exist for all three categories in every patient. Improvement in the course of the disease, as assessed by level of blood pressure, presence of symptoms, physical findings, and functional capacity, was greatest in Groups III, IV, and V—that is, in those patients who had a sustained therapeutic relationship with the physician. The period of observation was, on the average, only 21 months, but there seemed to be little doubt that most patients experienced relief of symptoms and were able to function more effectively, and that with the improved state there was usually lack of objective evidence of progression of the disease. In a few patients some regression of structural changes and blood pressure level was seen.

The increase in frequency of observed correlations between stress-producing situations and the course of the illness with increased intensity of study of the patient implies that such correlations are probably commoner than a superficial examination would suggest. In the same way, it would seem that the therapeutic relationship is more effective when the physician has thorough knowledge of the patient's emotional problems and can help him to deal with them. *Desmond O'Neill*

See also Digestive Disorders, Abstract 2020.

2093. Inheritance of Manic-depressive Psychosis

D. J. MERRELL. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 66, 272-279, Sept., 1951. 11 refs.

The diagnosis of manic-depressive psychosis is shown statistically to be less common than formerly, and the definition of the psychosis can be assumed to be less inclusive than before. Figures on discharges and readmissions confirm the cyclical nature of the psychosis. Evidence that women are more severely affected than men is to be found in the earlier age of onset and of first admission and in the greater proportion of affected women. Data on twins show conclusively that heredity is involved in the etiology of the psychosis.

The high incidence of the manic-depressive psychosis among the relatives of persons with this psychosis and the difference in frequency of the psychosis in different populations are further evidence for the role of heredity. The frequency of the psychosis is about the same among the parents, sibs, fraternal twins, and children of patients with manic-depressive psychosis. The best genetic explanation for the data is that of a single autosomal dominant gene with incomplete penetrance.—[Author's summary]

2094. Psychiatric Implications of the Treatment of Alcoholism with Tetraethylthiuram Disulfide. A Preliminary Report

B. H. GOTTESFELD, L. M. LASSER, E. J. CONWAY, and N. M. MANN. *Quarterly Journal of Studies on Alcohol* [Quart. J. Stud. Alcohol] 12, 184-205, June, 1951. 11 refs.

The implications of the treatment of alcoholism with tetraethylthiuram disulfide (TETD) are discussed, based on experience with 42 patients at the Blue Hills

Clinic of the Connecticut Commission on Alcoholism. In 8 patients psychotic episodes developed. Many people take alcohol as a defensive tactic, a pleasure equivalent, a relief from tension of any kind, and to engender a feeling of harmony and well-being. Over-indulgence in alcohol tends to give rise to dependency and secondary complications in the individual; the withdrawal of alcohol and the often unpleasant physiological effects of TETD might be expected to create another stressful condition necessitating substitute forms of relief. The meaning and significance of the drug to the patient have been found to be of special importance. Before treatment a careful physical and psychiatric survey is made and, when possible, a Rorschach test carried out. Psychotherapy is part of the treatment and the patient is under observation either in hospital or as an out-patient. The psychotic episodes in 8 patients followed a similar pattern: initial complaint of drowsiness and inability to work, gastro-intestinal symptoms, followed by anxiety and amnesia, depression, hostility, and restlessness; in the worst cases schizophrenic paranoid manifestations were present. In 5 the psychotic episodes were transitory and responded quickly to withdrawal of TETD and to sedatives; in 3 they were more serious and required continued special treatment.

It was concluded that projective, hostile individuals who find interpersonal relationships difficult to form, and those with a psychotic history, are unsuitable for TETD treatment. Individuals who are able to utilize psychotherapy and to develop sustained interpersonal relationships and who show utilizable dependency traits, and those who have a recognized need for sobriety to make them acceptable at work and at home, are likely subjects for successful treatment. It is also considered that further psychiatric, medical, and physiological studies are necessary for correct evaluation of all the factors concerned. *Myra Mackenzie*

2095. Psychotic Phenomena Provoked by Tetraethylthiuram Disulfide

O. MARTENSEN-LARSEN. *Quarterly Journal of Studies on Alcohol* [Quart. J. Stud. Alcohol] 12, 206-216, June, 1951. 4 refs.

Psychotic phenomena provoked by tetraethylthiuram disulfide (TETD) are described, and illustrated by 6 cases presenting common features which indicated TETD as the provoking agent. Of the 6 patients 5 were alcoholics. One, a young pregnant woman, though not an alcoholic, was of infantile psychic make-up with light paranoid ideas; as her mental condition was deteriorating it was considered advisable to try to terminate the pregnancy by TETD. The symptoms common to all 6 cases were initial sleepiness, tiredness, or drowsiness with indisposition to work, and, later, increasing disorientation, amnesia, and anxiety with insomnia which might become restlessness so violent as occasionally to require physical restraint. In some cases a paranoid equivalent appeared; one patient became megalomaniacal.

From the beginning the daily dose of TETD varied from 1.5 to 3.0 g., and most patients denied taking any alcohol between the initiation of treatment and the

manifestation of psychosis. From the experience gained in treating over 1,300 patients with TETD the author considers that if the dosage is not unnecessarily high, and if the patient is observed continuously for the relatively mild symptoms pointing to commencing psychosis, this undesirable complication may be avoided. Provided the patient is not under the influence of alcohol when first seen, 0.02 g. of TETD per kg. of body weight should be given at once; on the evening of the same day, and on the following 5 days, one-third the initial dose is given. If any pronounced side-effects are noted on examination on the fifth day the daily dose is reduced. A similar examination is made every 5 days while treatment continues. In this way it should be possible to find a mean between the therapeutic and the "toxic" dose for any patient.

Myra Mackenzie

See also Digestive Disorders, Abstract 2008.

2096. **A Non-mutilating Form of Intracerebral Treatment.** (Une thérapeutique intracérébrale non mutilante)
P. ABELY and P. GUYOT. *Presse Médicale* [Pr. méd.] 59, 1010-1011, July 14, 1951.

Recognizing the therapeutic effects of leucotomy and related procedures in improving psychotic states, yet regretting the mutilating character of these operations, the authors have developed an injection technique to serve the same purpose. This differs from the early Moniz method of injecting necrosing substances (chemical lobotomy), for bland fluids are used. Examples mentioned are isotonic and hypertonic glucose saline, calcium, vitamins B and C, methionine, oxygen, and "nicyl". The injection used is chosen to accord with the nature of the case. The indications for each therapeutic agent, and also the results obtained, are not reported, but will be published later. Injection is carried out with a needle similar to that used for lumbar puncture, but graduated in centimetres. Burr-holes are first made in the usual position for leucotomy operations, and the injections are delivered into the centrum ovale.

Donald McDonald

2097. **Epilepsy and Prefrontal Lobotomy.** (Epilepsie et lobotomie préfrontale)
—, FEUILLET, —, COLLINS, M. THIEBAUX, and R. THIEBAUX. *Archives Internationales de Neurologie* [Arch. int. Neurol.] 70, 62-71, April, 1951. 25 refs.

Epilepsy is one of the most frequent complications, though not the most serious, following brain surgery. The reported incidence of seizures after lobotomy varies: a rough average would be 6% to 12%. The symptoms are generalized convulsions without aura or other prodromal symptoms, and are usually temporary. Of the 11 cases described by the present authors in which seizures occurred after prefrontal lobotomy 3 had 1 seizure, 2 had 2, 3 had 3, and 3 had more than 3; the first seizure occurred 9 to 19 months after operation, thereafter recurring at intervals of 3 to 6 months. True epilepsy is very rare in such cases, is usually related to cerebral tumours, and occurs mostly in children and defectives. Of the patients observed, 8 were schizo-

phrenic, 2 manic-depressive, and 1 oligophrenic; all 11 patients were comparable in their condition and age to other lobectomized patients observed who had no seizure.

Of the surgical techniques in current use that of closed lateral lobotomy (Freeman and Watts) shows the lowest, and that of transorbital lobotomy the highest, incidence of post-operative seizures. Pre-operative electroencephalographic records do not predict any significant proneness to post-operative attacks. Prognosis is usually good; seizures generally disappear spontaneously after about 2 years, and treatment of stubborn cases is usually successful. The influence of prefrontal lobotomy on patients already suffering from epilepsy is slight in that, if seizures cease completely, relief is usually temporary. They may, however, be reduced in gravity and/or frequency. The authors have noted only one case of complete cure. Concomitant personality disorders and psychotic symptoms may be considerably relieved by operation whether or not the seizures are affected.

N. A. Standen

2098. **Treatment of Psychoneurosis. Modified CO₂ Abreactive Technique**
W. L. MILLIGAN. *British Medical Journal* [Brit. med. J.] 1, 1426-1428, June 23, 1951. 6 refs.

Following the employment in recent years of drugs and gases as aids to psychiatric therapy, the author has used a modified form of Meduna's technique for administering carbon dioxide to facilitate the process of abreaction. The patient, treated in bed in a quiet room, has the procedure briefly explained to him. From a mask he inhales at first pure oxygen, then a mixture in which the proportion of carbon dioxide rises gradually from 10% to 15%; after the patient has taken 20 breaths the carbon dioxide is suddenly increased to 30% and immediately lowered to the earlier level; after a further 25 to 40 respirations the inhalation is rapidly stopped. The concentration of carbon dioxide varies with the individual, but should be sufficient to produce overbreathing with some restlessness. When the mask is removed abreaction may follow immediately, but usually occurs after about half an hour's reminiscence.

Of the 40 patients treated (mainly suffering from hysteria and anxiety states with obsessional features) all benefited considerably, the number of treatments varying from 2 to 12 and a complete cure being effected in some cases. Compared with many abreactive techniques, this has the following advantages: it is safe and, being followed by no unpleasant after-effects, it is suitable for out-patients; it is technically simple; the patient remains conscious throughout; incidents are recalled with clarity and repressed material easily released. Partial resistance arising during the interview may be overcome by administering a few additional breaths of 20% carbon dioxide.

N. A. Standen

2099. **The Treatment of Psychoneurotics. Some Practical Considerations**
W. L. NEUSTATTER. *Lancet* [Lancet] 1, 1331-1334, June 23, 1951. 6 refs.

Infectious Diseases

2100. **Generalized Torulosis.** (Generalisierte Torulose) G. BRUNS. *Zentralblatt für Allgemeine Pathologie und Pathologische Anatomie* [Zbl. allg. Path. path. Anat.] 87, 360-364, July 20, 1951. 3 figs., 34 refs.

A detailed description, with 3 photomicrographs, is given of a case of torulosis due to *Cryptococcus neoformans*, in which small "tumours" made up of fungi were found in the meninges, including the dura, and in the glomeruli of the finely granular kidneys. The patient, aged 71, had had symptoms which suggested a diagnosis of cerebrospinal syphilis, although no actual signs could be found.

[The only other case with localization in the dura appears to be that reported by Semerek (*Arch. Path.*, 1928, 6, 1142).]
L. Michaelis

2101. **Recent Investigations into the Treatment of Schistosomiasis by Miracil D in Egypt**

J. NEWSOME. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. R. Soc. trop. Med. Hyg.] 44, 611-634, June, 1951. 8 refs.

Owing to the difficulty of preventing reinfection in patients, most of the work reported here was performed on prisoners, who were kept under close observation. As the hydrochloride of "miracil D" is toxic, other salts were also used. Of these the methylene bis-hydroxynaphthoate was given in *Schistosoma haematobium* infection in doses varying up to 1.5 g. twice daily for 3 days, then 1.0 g. twice daily for a further 3 days. It proved less toxic than the hydrochloride but, owing to its insolubility, insufficient of the drug was absorbed to be very effective, even when given with tincture of opium. The salicylate was then tried on a small series of cases; toxic reactions were slight and a blood concentration of greater than 4 µg. per ml. was obtained in 5 soldiers who received the equivalent of 100 mg. of the hydrochloride per kg. body weight. It appeared to be superior to the other salts. The rate of cure was 23 out of 50 patients given miracil and its derivatives.

Infections with *Schistosoma mansoni* were treated with the hydrochloride, usually in two short courses. Colic and vomiting occurred. The cure rate, assessed by routine measures, was 19 out of 29; assessed by more strict methods it was considerably less. These methods consisted of hatching eggs from both urine and faeces and of biopsy of rectal mucosa. The latter test brought to light many *S. haematobium* infections in which egg-free urine was passed. In a survey of a village 247 clinical cases were detected. In 133 of these examinations of urinary deposit revealed *S. haematobium* eggs. The urine hatching test was positive in another 28; rectal scrapings were positive in 221 cases; the final figure was 236 confirmed cases out of 247.

The author states that although the results obtained with miracil D are disappointing, the drug may not be

inferior to others, for the tests of cure were more stringent than in many other trials. The naphtholate may be effective in other countries where the infections are less heavy, and it should not be condemned on the basis of the present trials.
W. H. Horner Andrews

2102. **The Use of Terramycin in Rocky Mountain Spotted Fever**

A. M. POWELL, M. J. SNYDER, J. V. MINOR, J. F. BENSON, and T. E. WOODWARD. *Bulletin of the Johns Hopkins Hospital* [Bull. Johns Hopk. Hosp.] 89, 30-38, July, 1951. 4 figs., 7 refs.

The authors report the results of treatment with terramycin of 7 representative cases of Rocky Mountain spotted fever as it occurs in Maryland [the causal agent *Rickettsia rickettsii* being, in this region, conveyed mainly by the tick *Dermacentor variabilis*]. Terramycin has already been used successfully in other rickettsial fevers and this series includes 2 cases of Rocky Mountain spotted fever previously reported (Bower *et al.*, *Ann. N.Y. Acad. Sci.*, 1950, 53, 395). There were 4 children, aged 3, 4, 7, and 12 years, and 3 adults, aged 27, 34, and 81. Clinical diagnosis was confirmed in every case by inoculation tests in guinea-pigs and serial Weil-Felix and complement-fixation reactions. The customary fatality rate of the disease in Maryland is approximately 21%, but all the patients in this series recovered. In 2 adults clinical response was poor or delayed and the blood level of terramycin not measurable. One of these patients (aged 34) was desperately ill and therefore intravenous chloramphenicol therapy was instituted, with satisfactory results. For this reason the authors exclude this case from further discussion. They add that terramycin hydrochloride for intravenous use is now available.

Terramycin (250-mg. capsules) was given orally in initial doses of approximately 50 mg. per kg. body weight; approximately 3.0 g. was given initially to adults, followed by 1.0 g. 8-hourly. Children received two-thirds of the adult dose. The optimum dosage is not yet determined. The antibiotic was continued until temperature returned to normal, provided there was concomitant clinical improvement. The mean day of disease on which treatment was started was 6.4. In 5 cases improvement occurred within 24 hours. On the second day headache, weakness, and mental dullness abated and by the third, patients were convalescent. Irrespective of the age of the patient, height of fever, or day of disease defervescence after the initial dose occurred in an average of 60 hours, whereas the average duration of fever in Maryland has hitherto been 15 days in children and 18 days in adults. Mild nausea, vomiting, and diarrhoea occurred in 3 cases, but did not interrupt therapy. Examination of urine showed no abnormality and there were no significant changes ascribable to the drug in the haemoglobin level

or blood picture. In 6 cases rickettsiaemia was demonstrated and also rising titres for *Proteus* OX 19 or OX 2 and complement-fixing antibodies. Sera examined at various time-intervals after administration showed a mean level of 5.4 μ g. of the antibiotic per ml.

The authors observe that the remarkable effectiveness of aureomycin and chloramphenicol in the treatment of Rocky Mountain spotted fever is well known and they conclude that terramycin must share in this effectiveness. They emphasize, however, that whatever the antibiotic used, sole reliance must not be placed upon it in patients who are seriously ill if the antibiotic is first given late in the course of the disease. Transfusions of saline, glucose, plasma, and whole blood are vital for the embarrassed circulatory system. [At least equally important is skilled nursing, without which all the efforts of the physician may fail.] E. H. R. Harries

VIRUS INFECTIONS

2103. **The Clinical Features of Psycho-sensory Encephalitis in Children.** (Клиническая характеристика психосензорного энцефалита у детей)
I. S. GLAZUNOV, T. A. SHUTOVA, and L. A. IVANOVA.
Невропатология и Психиатрия [*Neuropat. Psikhiat.*] 20, No. 2, 17-21, 1951.

Since 1947 the authors have collected 200 cases of an infective nervous disease characterized by an initial short febrile illness followed by a prolonged period of paroxysmal psycho-sensory attacks. A more detailed study was made of 100 of these cases, and this forms the basis for the present account of the clinical features.

The majority of the patients were children between 8 and 10 years of age, but several cases occurred in families and some of these were in adults. The initial acute period of the disease, which lasted from 2 to 5 days, resembled influenza and was marked by pyrexia, headache, coryza, malaise, and lassitude. Occasionally nausea, vomiting, and disturbances of sleep were also observed during this stage. The second period usually began 2 to 3 weeks later. It was characterized by anorexia, enlargement of the peripheral lymph nodes, and some swelling and tenderness over the liver. Most of the children were found to have ascariasis. In 25% of the patients there was leucocytosis, and in the remainder eosinophilia and lymphocytosis. The patients frequently complained of headache and had occasional attacks of vertigo. The psycho-sensory phenomena occurred at this stage, and they may be described as defective synthesis between the environmental and the bodily sensations. A difficulty was experienced in reading and writing: syllables were omitted and letters doubled. External objects and parts of the patient's body appeared to move and to fade from sight. Visual and auditory sensations varied in intensity; diplopia occurred, and micropsia or macropsia was sometimes present. The disturbances of sensation were in some cases accompanied by light and transient neurological signs, such as inequality of the pupils, congestion, and, more rarely, oedema of the disks, central facial paralysis,

nystagmus, Rombergism, vestibular disturbances, and paresis of the hypoglossal nerve. Muscle tone was lowered; choreiform and athetoid movements were present in 10 cases; the plantar reflexes were absent in 10 cases and were pathological in 25; a positive Kernig sign was elicited in 5 cases. Electroencephalographic abnormalities were observed in 62% of the patients; they included disorganization of the alpha rhythm and the appearance of waves with a frequency of 4 to 6 per second. The cerebrospinal fluid was normal, but its pressure was often raised. Emotional instability was sometimes seen during this period, but there was never any intellectual deterioration. There were no fatal cases in this series.

A virus was isolated from the patients and inoculated into monkeys. The pathological findings in the monkeys consisted of "inflammatory changes in the meninges and the vascular plexuses of the brain". The cells in the inflammatory infiltrate were mainly monocytes and, to a lesser degree, plasma cells and lymphocytes. There was oedema of the periventricular white matter.

The lesions in the human cases were transient and appeared to be situated chiefly in the brain stem. A suitable name for the disease is "chorio-encephalitis".

L. Crome

2104. **The Clinical Features and the Course of Spring-Summer Encephalitis in the Epidemiological Foci of the Eastern and the Western Regions of the U.S.S.R.** (Клиника и течение весенне-летнего энцефалита в его очагах в восточных и западных районах)
A. G. PANOV. Невропатология и Психиатрия [*Neuropat. Psikhiat.*] 20, No. 2, 29-36, 1951.

The clinical features of an epidemic of spring-summer encephalitis observed by the author in one of the eastern regions of the Soviet Union are compared with those studied by other workers in one of the north-western regions. Viruses were isolated in both of the epidemics and proved to be identical. While there was a certain difference in the relative frequency of the neurological syndromes observed in the two epidemics, the course and the symptomatology were sufficiently similar for the disease to be considered as one nosological entity.

L. Crome

2105. **The Nature of the Tick-borne Encephalitis Occurring in Bielorrussia.** (К вопросу о природе клещевого энцефалита встречающегося в БССР)
N. I. GRASHTCHENKOV, A. M. GURVITCH, and L. V. FEDORTCHUK. Невропатология и Психиатрия [*Neuropat. Psikhiat.*] 20, No. 2, 36-46, 1951.

Cases of tick-borne encephalitis are infrequent in Bielorrussia. They have, nevertheless, become the object of considerable interest since it was shown by Zilber and Shubladze that they differ from the tick-borne encephalitis found elsewhere in the Soviet Union and are identical with "Scottish encephalitis" (human louping-ill). This view has been challenged by other Soviet workers, who claim that the virus in all such cases is identical. No general agreement has been reached and an expedition consisting of clinicians, virologists, and parasitologists

was therefore organized in the summer of 1950 to study this problem in Bielorrussia. This expedition collected 7,000 ticks, 99% of which were *Ixodes ricinus* and 1% *Dermacentor pictus*. [The tick concerned in the transmission of the disease in the Far East is *Ixodes persulcatus*.] Three strains of neutotropic virus were isolated from the ticks by means of inoculation into white mice. The virus was then inoculated subcutaneously and intracerebrally into sheep. All the sheep which were inoculated intracerebrally developed louping-ill, and the virus was recovered from their brains.

Three human subjects were reported to the expedition as suffering from tick encephalitis. These cases were carefully investigated and it was found that clinically the disease was indeed very similar to human louping-ill. The attempt to isolate the virus from these cases during the second stage—that is, the meningo-encephalitic phase of the disease—proved, however, unsuccessful. (The follow-up of serum antibody levels is still continuing.)

No spontaneous cases of louping-ill were found among the sheep in the investigated district.

It is concluded that in districts inhabited by *Ixodes ricinus*, tick encephalitis is very similar to louping-ill. In areas inhabited by both *I. ricinus* and *I. persulcatus* encephalitis may be either of the louping-ill or of the Far-Eastern type. In areas inhabited solely by *I. persulcatus* encephalitis is of the classical Far-Eastern type and is characterized chiefly by poliomyelitic syndromes. The authors point out that the evidence is not yet complete and that it remains necessary to isolate the virus from the human cases, and also to explain the reasons for the absence of spontaneous louping-ill in the district investigated by the expedition.

L. Crome

2106. The Clinical Picture and the Histopathology of a Type of Haemorrhagic Fever Observed in the Bukovina. (К клинике и гистопатологии заболевания типа геморрагической лихорадки на Буковине) S. N. SAVENKO and Y. G. RUZIONVA. Невропатология и Психиатрия [Nevropat. Psikhiat.] 20, No. 2, 56-60, 1951.

A peculiar type of haemorrhagic fever occurred in the Bukovina in the summers of 1947 and 1948. Most of the 36 patients gave a history of a sojourn in forest country and of receiving tick-bites. A virus was subsequently isolated from them.

The illness was marked by a 7-day continuous fever, pronounced weakness, lumbar and leg pains, headache, disturbances of consciousness, and meningeal symptoms. Congestion and bleeding from the mucous membranes occurred frequently. An initial leucocytosis was often followed by leucopenia; thrombocytopenia was observed in a few cases. Disturbances of the somatic and the vegetative nervous system were present in all cases. Of the total number of patients 8 died. Three patients who recovered showed considerable cerebral, cerebellar, extrapyramidal, and mental signs. Another 13 showed meningeal signs and brain-stem and pyramidal disturbances, with some residual signs after recovery. The remaining patients had no meningeal symptoms, but some neurological signs could be elicited on examina-

tion. The pathological findings in the fatal cases were hyperaemia and haemorrhages in the meninges, and widespread haemorrhages in the gastro-intestinal tract, lungs, and splenic capsule. Microscopically, the brain showed stasis, haemorrhages, and exudation of plasma from the small cerebral blood vessels. A slight lymphocytic infiltration was present in the perivascular spaces. Diffuse proliferation of micro- and oligo-dendroglia could also be seen. These changes were present throughout the brain, but were more marked in the midbrain, pons, putamen, and in the cerebral cortex.

Other cases of tick-borne encephalitis are found in Bukovina but are clinically different from those described above. Crimean haemorrhagic fever is not associated with such pronounced involvement of the nervous system. The disease resembles most the Japanese mosquito-borne encephalitis, from which it can only be distinguished by virological study.

L. Crome

2107. The Clinical Features of the Serous Meningitis Associated with Epidemic Parotitis. (К клинике серозного менингита при эпидемическом паротите) G. KIRKEVITCH and R. Z. INSAROVA. Невропатология и психиатрия [Nevropat. Psikhiat.] 20, No. 2, 12-16, 1951. 2 figs.

Serous meningitis associated with mumps was studied in 52 cases. The patients were mostly school children and the number of boys was three times that of girls. In 37 patients parotitis was concurrent, in 7 it was abortive, and 8 had only a history of contact with mumps and no clinical parotitis.

The meningitic stage was acute in onset, lasting 4 to 5 days, and in 10 cases ran a rather difficult clinical course with some encephalitic signs. The cerebrospinal fluid showed an increase of cells amounting to about 150 to 300 lymphocytes per c.mm., protein content was raised to 66 to 99 mg. per 100 ml., and pressure was normal or low.

The differential diagnosis of the condition is discussed.

L. Crome

2108. Studies on the Prevention of Mumps—I. The Determination of Susceptibility

G. HENLE, W. HENLE, J. S. BURGOON, W. J. BASHE, and J. STOKES. Journal of Immunology [J. Immunol.] 66, 535-549, May, 1951. 18 refs.

Skin tests with mumps virus grown in the chick allantoic cavity and inactivated with ultraviolet light have been carried out on 1,853 persons and complement-fixation tests with V antigen on 1,556, and the results correlated with history of mumps infection previous and subsequent to the tests.

In the skin tests 0.1 ml. of antigen (10^7 ID 50 per ml.) was injected intracutaneously, using uninoculated allantoic fluid as control, and the reactions were read 24 to 36 hours later: an erythematous area of an average diameter of 15 mm. or more was considered positive, one 10 to 14 mm. in diameter doubtful, and one less than 10 mm. in diameter negative. In complement fixation tests a titre of 1 in 2 (original dilution) was regarded as positive.

Both tests gave fair correlation with previous history of mumps infection, though, especially in persons under 18 years, experience of mumps was often associated with a negative skin reaction. The high proportion of people who showed a positive reaction in either or both tests without a history of mumps is explained as being due to subclinical mumps infection. Subsequent infection with mumps appears much commoner in persons with a negative skin or complement-fixation reaction, and is commoner still in persons in whom both tests are negative than in persons in whom both tests are positive.

The authors recommend the use of both tests in determining the treatment of contacts and in deciding on the need for immunization.

C. L. Oakley

2109. Studies on the Prevention of Mumps—II. The Effect of Skin Testing upon Antibody Level and Resistance G. HENLE, J. S. BURGOON, W. J. BASHE, C. F. BURGOON, J. STOKES, and W. HENLE. *Journal of Immunology* [*J. Immunol.*] **66**, 551–560, May, 1951. 2 figs., 10 refs.

Intracutaneous injection of 0.1 ml. mumps virus grown in the chick allantoic cavity and inactivated with ultraviolet light produced an increase of complement-fixing and haemagglutination-inhibiting antibodies in a proportion of persons injected. The proportion depends on the age of the group: while 75% of adults reacted, there were only 23% reactors among children between 0 and 5 years. The authors suggest that this is due to the possession by older persons of some basal immunity as a result of which the skin injection acts as a booster dose, whereas in young children the skin test acts as a primary stimulus.

Skin testing had no effect on the incidence of mumps in several institutions: the incidence in skin-tested and control groups was much the same.

C. L. Oakley

2110. Studies on the Prevention of Mumps—III. The Effect of Subcutaneous Injection of Inactivated Mumps Virus Vaccines

G. HENLE, W. J. BASHE, J. S. BURGOON, C. F. BURGOON, G. R. HUNT, and W. HENLE. *Journal of Immunology* [*J. Immunol.*] **66**, 561–577, May, 1951. 12 refs.

Subcutaneous injection of mumps virus grown in the chick allantoic cavity, concentrated about 20 times and inactivated with formalin or ultraviolet light leads to an increase of complement-fixing and haemagglutination-inhibiting antibodies in a proportion of people. This proportion depended on the volume of virus injected: a dose of 4 ml. was necessary to produce a response in all persons injected. The maximum titre was reached in 2 to 3 weeks. Reactions were trifling. As the ratio between complement-fixing and haemagglutination-inhibiting antibodies is not constant it is concluded that the two methods measure different antibodies.

In an epidemic of mumps that occurred no less than 9 months after immunization the incidence in the immunized was about half that in the controls, and seemed to bear a definite relationship to the complement-fixing-antibody titre. No proved case of mumps occurred in any of the 33 people who had a titre of 1 in 16 or more in this test after immunization.

C. L. Oakley

2111. Studies on the Prevention of Mumps—IV. The Effect of Oral Spraying of Attenuated Active Virus

G. HENLE, J. STOKES, J. S. BURGOON, W. J. BASHE, C. F. BURGOON, and W. HENLE. *Journal of Immunology* [*J. Immunol.*] **66**, 579–594, May, 1951. 5 figs., 15 refs.

Oral spraying of children judged to be susceptible to mumps with 0.5 ml. active allantoic-cavity mumps virus ($10^{7.5}$ to $10^{8.9}$ ID₅₀) led to increase in complement-fixing antibodies in 93% and to mild signs of mumps infection in 1.5%. If the virus was diluted 10-fold to 100-fold before spraying, the proportion of those responding fell to 50% and less than 10% respectively. As, after oral spraying, antibodies to the S antigen frequently attain higher levels than those against the V antigen—a finding comparable with that following mumps infection, but the reverse of what occurs after subcutaneous injection of inactivated virus—the authors consider that the effect of spraying active virus is the production of an inapparent mumps infection. Spraying inactivated virus does not elicit any antibody response. In most instances no circulating antibody could be detected a year after spraying, but sprayed children gave a larger antibody response to skin tests than did the controls, showing that the sprayed children possessed a basal immunity.

Experimental exposure to active mumps virus of 4 sprayed children 3 months after spraying failed to produce any signs of mumps infection: 4 out of 6 controls developed mild mumps. Experience in the field is too slight for definite conclusions, but seems sufficiently favourable to justify further experimental work.

C. L. Oakley

2112. A Familial Epidemic of Pleurodynia (Bornholm Disease). (*Epidemia familiare di pleurodinia (Malattia di Bornholm)*)

G. BAGGIO. *Acta Paediatrica Latina* [*Acta paediatr. lat., Padova*] **4**, 321–337, July-Aug., 1951. 1 fig., 23 refs.

An outbreak of an acute febrile disease, characterized by intense pain in the lower part of the chest and adjacent part of the abdominal wall, aggravated by respiration, voluntary movements, or local pressure, is described. Eight children and a servant in two related families were affected out of a total of 13 persons. The families lived at Noventa, near Padua, and at Verona, the infection apparently being carried from the first family affected to the second by a member of the latter family returning home after a visit of some days. The first case in each family arose within 2 days of each other. All the patients were taken ill within 7 days, the incubation period being about 2 days. Full details of each case are given. The author considers the disease to be epidemic myalgia (Bornholm disease), which, although well recognized in Northern Europe, is not so well known in Italy.

In order to show how his cases fit the diagnosis the author goes on to discuss the disease under various headings, such as history, incubation time, method of spread, causative agent, symptomatology, complications, differential diagnosis, and treatment. With each section there is a review of most of the previous work on Bornholm disease.

[The main object of this paper is to draw attention to epidemic myalgia in Italy, but the review is full enough to be useful to workers in other countries.]

R. F. Jennison

2113. Upper-respiratory Infection as a Factor Influencing Susceptibilities to Poliomyelitis

T. H. INGALLS and W. L. AYCOCK. *New England Journal of Medicine* [New Engl. J. Med.] **245**, 197-203, Aug. 9, 1951. 7 figs., 25 refs.

In 1936 an isolated and localized outbreak of poliomyelitis occurred in an American boys' school. Of the 190 boys 22 showed symptoms of paralysis after an upper respiratory infection had developed among 52 scholars of this school a month before the poliomyelitis occurred. The interval between the times of onset of the two types of illness ranged from 4 to 22 days and averaged about 9½ days.

Franz Heimann

2114. The Relation of Sex, Pregnancy and Menstruation to Susceptibility in Poliomyelitis

L. WEINSTEIN, L. AYCOCK, and R. F. FEEMSTER. *New England Journal of Medicine* [New Engl. J. Med.] **245**, 54-58, July 12, 1951. 2 figs., 19 refs.

An analysis of 550 cases of poliomyelitis admitted to the Haynes Memorial Hospital, Boston, in 1949 and 1950 showed that of 108 female patients between the ages of 20 and 40, 26 (24%) were pregnant. It was calculated from the birth rate that 7% of women in this age group would be expected to be pregnant at a given time, and it was therefore concluded that pregnancy increases the susceptibility to poliomyelitis. It was found that while women who develop the disease early in pregnancy and are convalescent at the time of delivery suffer no ill-effect, parturition in the acute phase increased the risk of extension of paralytic manifestations. About 75% of women patients with poliomyelitis have a menstrual period from 5 days before to 4 days after the onset of the first symptoms of the infection.

The above observations suggest a possible influence of sex hormones or other endocrine substances on the pathogenesis of the disease.

R. S. Illingworth

2115. Tonsillectomy and Adenoidectomy and Poliomyelitis

A. H. MILLER. *Archives of Otolaryngology* [Arch. Otolaryng., Chicago.] **53**, 160-169, Feb., 1951. 2 refs.

The results of a very careful statistical examination of the possible relationship between the tonsil and adenoid operation and the occurrence of poliomyelitis are thus summarized by the author in a paper read before the Otorhinolaryngological Section of the American Medical Association: "A survey of the 1,229 cases of poliomyelitis occurring in the Los Angeles County during the epidemic year 1949 has been presented in an attempt to determine whether there is any relationship between a recent tonsillectomy and adenoidectomy operation and (1) the incidence of poliomyelitis and (2) the development of bulbar poliomyelitis, as well as in an attempt to determine whether (3) tonsillectomies and adenoidectomies

should be discontinued during the summer months of highest poliomyelitis incidence. The results of the statistical analysis indicate no clinical or statistical deviation between the actual and expected incidence of poliomyelitis developing in Los Angeles County during 1949 in patients recently tonsillectomized and adenoidectomized, even in the months of July through October. In view of these observations, there seems to me to have been no reason found to discontinue doing indicated tonsillectomies and adenoidectomies during the summer months."

(In the subsequent discussion there seems to have been general agreement with the author. Martin referred to "emotion and hysteria fostered by popular publications". If there were no epidemic he would continue to operate during the summer months; if there were an epidemic he would not operate. Goodhill, also agreeing with the author, said that it had been necessary to advise curtailment of essential procedures simply to avoid censure by the lay public "aroused by unwarranted sensational press propaganda". Lamb, as a paediatrician, emphasized the importance of taking all the child's circumstances into account. Leake felt that any increase of incidence by elective operation was very small. Harkness made the interesting point that during an epidemic in Iowa 25 years ago he was asked by Resnow, who was investigating the outbreak, to remove the tonsils of all patients who had been in contact with poliomyelitis during the epidemic; so far as he knew none of those patients developed poliomyelitis.)

F. W. Watkyn-Thomas

See also Hygiene and Public Health, Abstract 1748; Microbiology, Abstract 1905.

BACTERIAL INFECTIONS

2116. Disturbances of the Locomotor System in Tularaemia. (О поражении органов движения при Туляремии)

I. R. DROBINSKII. *Клиническая Медицина* [Klin. Med., Mosk.] **29**, No. 6, 85, 1951.

In a series of cases of tularaemia [numbers unspecified] the author has observed in 4% objective changes in the bones and joints, especially polyarthritis, developing usually from the 10th to 15th day of the disease, when granulomata and well-marked allergic changes are present.

In all of these cases the subcutaneous test for tularaemia was strongly positive; and often a polymorphous exudative or nodular erythema, endocarditis, pneumonia, or granulomatous conjunctivitis accompanied the arthritis, which was twice as common in the bubonic as in the visceral form of the disease. The arthritis was usually of the serous type, but in some cases was suppurative, leading to ankylosis. The joints most commonly affected were the radio-carpal, metacarpophalangeal, tibio-astragaloid, and knee-joints. The arthritis lasted from 3 to 5 weeks. The erythrocyte sedimentation rate was much increased; leucopenia was the rule. More rarely, the locomotor disturbances were

of the nature of bursitis, monoarthritis, suppurative chondritis, or diffuse myositis with muscular spasm. The most effective relief was obtained by giving "pyramidon" (amidopyrine), 30 gr. (2 g.) daily for 5 days, sodium salicylate, 150 to 300 gr. (10 to 20 g.) daily for 2 weeks, or aneurin bromide by subcutaneous injection, 50 mg. per day.

L. Firman-Edwards

2117. Antibiotic Treatment of Pertussis. Comparison of Penicillin, Aureomycin, Chloramphenicol, and Terramycin in 150 Cases

L. N. HAZEN, G. G. JACKSON, S.-M. CHANG, E. H. PLACE, and M. FINLAND. *Journal of Pediatrics [J. Pediat.]* 39, 1-15, July, 1951. 3 figs., 4 refs.

The authors report on investigations dealing with clinical and bacteriological observations and the effects of four different antibiotics. A series of 150 patients whose ages ranged from 4 weeks to 11 years were divided into four groups, each group receiving, respectively, aureomycin, chloramphenicol, terramycin, or penicillin in oral doses of 60 mg. per kg. per day for 10 days. The first three antibiotics produced rapid clinical improvement; the number of paroxysms of coughing decreased, cyanosis and vomiting subsided, and the appetite returned; bacteriologically, *Haemophilus pertussis* could not be isolated on or after the third day. On the other hand, the treatment with penicillin had a much slower effect both clinically and bacteriologically; cultures of *H. pertussis* might still be positive after 4 weeks. According to the authors the time spent in hospital was longer in the penicillin-treated group than in those treated with the other drugs.

Franz Heimann

TUBERCULOSIS

2118. The Antisocial Tuberculous Patient. (Über asociale Tuberkulose)

H. BIRKHÄUSER and M. STOLL. *Schweizerische Zeitschrift für Tuberkulose [Schweiz. Z. Tuberk.]* 8, 79-98, 1951.

The authors analysed the personal and social histories of 65 so-called antisocial tuberculous patients, selected from 120 showing asocial tendencies. They constituted 5% of the total material of the Basle Tuberculosis Dispensary. The antisocial behaviour was characterized by rejection of adequate treatment, by serious offences against sanatorium rules and discipline, and by careless and frivolous neglect of hygienic precautions, resulting in infection of their contacts.

The investigation is concerned with the question how far this antisocial and abnormal behaviour is due to adverse environmental factors and the severe psychological shock caused on learning that they were suffering from tuberculosis, or how far the abnormal and unreasonable reaction to the disease is explained by a pre-existing psychopathic personality. The material was obtained from questionnaires answered by the patients, and corroborated and supplemented by detailed information from the files of the dispensaries, welfare

institutions, psychiatric clinics, and court records. Of the 65 histories so obtained 10 representative case histories are reported in full detail.

Of 65 patients 51 were social misfits or psychopathic personalities before contracting the disease. These people are a great public menace and adequate legal powers for the health authorities are required to deal effectively with them, to prevent the further spread of tuberculosis among the community. Of the 25 cantons in Switzerland 9 have already made adequate provisions for compulsory isolation if and where necessary.

An interesting sidelight is thrown on the pathogenesis of tuberculosis by the observation that in 51 of the 65 cases tuberculosis developed only after the patient found him- or herself in a difficult situation. Conflict situations are conspicuous in this series and it is statistically significant that in 45 cases psychological or mental abnormalities figure as the most important factor contributing to the conflict situations.

E. G. W. Hoffstaedt

2119. Tuberculosis among University Students, Resident Medical Officers and Probationer Nurses at the Cantonal Hospital in Lausanne. (La tuberculose chez les étudiants de l'université, les internes et les élèves-infirmières de l'Hôpital cantonal, à Lausanne)

A. DELACHAUX and G. THILO. *Praxis [Praxis]* 40, 246-249, March 22, 1951. 3 figs., 7 refs.

From 1934 to 1948 a total of 102 cases of tuberculosis was found among the university students, resident medical officers, and nurses at the Cantonal Hospital, Lausanne. The average annual number of students was 1,150, 350 in the faculty of medicine and 800 in other faculties; 42 cases occurred among the medical students and 60 among other students. The morbidity rates for the younger medical students in their first five semesters and for students of other faculties were closely similar. Among the older medical students in their last five semesters the morbidity was about 7 times as high, while the number of negative Mantoux tests in this group decreased from 26% to 7% during the student period. Thus, nearly 80% of these students were infected within about 4 years. Among the nurses the morbidity was even more marked, but from the beginning of 1947, when those who did not respond to tuberculin were inoculated with B.C.G., no more cases of tuberculosis were encountered among the new entrants.

P. C. Gugelot [*Excerpta Medica*]

2120. Results of Re-examination by Mass Radiography

V. H. SPRINGETT. *British Medical Journal [Brit. med. J.]* 2, 144-148, July 21, 1951. 7 refs.

The author analyses the results of repeated mass radiography of previously "normal" individuals. The 31,475 males and 15,013 females are divided into 5 age groups from 15 years upwards. As this series was started in 1946, the lowest age group in males is small, since these young men were in the Services till 1947. Even so, the highest incidence of new active lesions is found in the lowest age group (4.7 per 1,000), the incidence steadily falling to 1.7 per 1,000 in the 45-59 age group. There were no new cases above this

age. The same trend, but even more marked, is found in females, the incidence being 6.8 per 1,000 among the considerably larger number of young women between 15 and 24 years, and falling rapidly to 0.7 per 1,000 at 45-59, with none above that age. Unfortunately the attendance rate from any of the surveyed groups of offices was "probably less than 50%".

The incidence of newly discovered cases on repeat examination is related to the time interval between the first and second examinations in terms of "mean intervals". From these [rather artificial] "mean intervals" "annual attack rates" are calculated. In these are not included cases in which symptoms had developed and which had been diagnosed therefrom. An analysis of the time interval between first and second examination "suggests that, while some cases undoubtedly occur shortly after a normal chest x-ray film, there is a period of lowered incidence of clinically manifest disease after mass radiography, extending over a period of one year for females and over the first 2 years for males." [The abstract has shown that tuberculosis may develop at any time after a normal x-ray film (*Lancet*, 1947, 2, 955).]

On re-scrutinizing the first miniature films of those showing active lesions on re-examination, it was found that in 21 cases in males aged 35 or more a "stable" lesion had been present at the first examination, while 14 males of this age with active disease had previously had a normal film. Comparative figures show a very similar trend of age-incidence of active lesions on first examination to that found on repeat examination in females—7.5 per 1,000, falling to 1.7 per 1,000—whereas the incidence in males was much the same in all age groups (6 to 7 per 1,000) on first examination. There is a definite parallelism between the age-incidence of active tuberculosis and the death rate from respiratory tuberculosis in females. But in males the death rate rises with the age from 0.36 per 1,000 to 1.18 per 1,000, in direct contrast to the incidence rate. "It is suggested that a considerable proportion of these fatalities (in males) are the result of breakdown of lesions that have been present for many years and probably acquired without major symptoms in young adult life 30 to 40 years ago."

E. G. W. Hoffstaedt

2121. Technique of Jelly (Tuberculin) Skin-testing. Comparison between Various Techniques and the Mantoux Test

J. D. LENDRUM. *British Medical Journal* [Brit. med. J.] 2, 148-151, July 21, 1951. 15 refs.

The author has carried out thousands of comparative tuberculin tests in order to determine the relative efficiency and reliability of various techniques of percutaneous testing compared with the Mantoux test with 10 tuberculin units (T.U.), equivalent to 0.1 mg., of old tuberculin (O.T.), and, where necessary, with 100 T.U. (1 mg.) of O.T. In the first three techniques (A, B, and C) a jelly containing 60% w/v PPD tuberculin was applied; in the fourth (technique D) the PPD tuberculin was replaced by O.T. In all tests the jelly was applied to the skin between the shoulder-blades and then covered with adhesive plaster. This was removed after

48 hours and the result of the test read 48 to 96 hours after application.

The variations in the technique were as follows: (A) The skin was first firmly rubbed with cotton wool soaked in acetone, but without producing an erythema. After cleansing, the skin was stroked 6 times with "flour" sandpaper before applying the jelly. (B) The same procedure as in A, except that the skin was rubbed so hard with the cotton wool as to produce an erythema. After that the procedure was as under A. (C) Here again an erythema was produced by hard rubbing with the cotton wool, but the treatment with flour-paper was omitted. (D) The same as under A, but PPD jelly was replaced by O.T. jelly.

Techniques A and B were more sensitive than C; technique B was superior to A. Technique D, however, (with O.T. jelly), was still more sensitive than B: of 154 cases which were positive to D, only 134 were also positive to B. Of the 20 cases D-positive and B-negative, 12 gave a positive reaction to Mantoux with 10 T.U.; 7 which were negative to 10 T.U. reacted positively to Mantoux with 100 T.U. The jelly test with O.T. (technique D) was thus the most sensitive percutaneous tuberculin test, giving results midway between the Mantoux tests with 10 T.U. and 100 T.U. This was confirmed in a large series by direct comparison between the O.T. jelly test (D) and the Mantoux test with 10 T.U. In over 3,000 cases so tested there was almost complete identity of results where the Mantoux reaction was positive. In 48 cases out of 1,878 the Mantoux reaction was negative while the O.T. jelly test was positive. Of these, 39 were re-tested with Mantoux in a strength of 100 T.U., and 36 gave a positive reaction to the stronger dose. [See also Dick, *Brit. med. J.*, 1950, 2, 141.]

E. G. W. Hoffstaedt

2122. Dependence of *Mycobacterium tuberculosis* on Streptomycin. (De la dépendance du *Mycobacterium tuberculosis* à la streptomycine)

J. COLETSOS. *Revue de la Tuberculose* [Rev. Tuberc., Paris] 15, 548-555, 1951. 1 fig., 21 refs.

The author discusses the problem of streptomycin dependence, suggesting that there may be: (1) strict streptomycin dependence, in which the drug constitutes an essential growth factor for the organism; (2) relative streptomycin dependence, in which the drug is a real but facultative factor; and (3) simple stimulation of the growth of the organism by streptomycin.

Out of 2,150 streptomycin estimations made by the author at the Institut Pasteur 1,440 were made in a large-scale experiment to discover the conditions necessary for the appearance of streptomycin-resistant bacilli; 980 streptomycin-resistant cultures were isolated, but in only one was there found what seemed a possible streptomycin dependence. When this organism was grown on Löwenstein-Jensen medium no colonies appeared either in the control tube or in that containing 1 unit of streptomycin per ml.; the tube containing 5 units of streptomycin gave a poor growth, but the tubes with 10, 20 and 50 units a good growth. On reinoculation into Dubos medium, growth occurred with the same intensity

in the control as in the streptomycin tubes, thus proving that this was not a strict dependence. The patient continued to receive streptomycin for a further month, and on two occasions the experiment was repeated, but without reproducing the original finding.

Four human strains of tubercle bacilli were grown for several months in Dubos medium with added streptomycin. They were then cultured on Dubos medium alone for 10 days, and re-inoculated on to Youmans or Löwenstein-Jensen medium containing various strengths of streptomycin. Two of the strains showed the phenomenon of stimulation on both media, and the other two responded similarly though less definitely.

The author concludes that dependence can be produced experimentally, but dependence is not a constant or progressive factor. Although the phenomenon shows itself in certain exceptional circumstances, the antibiotic can be considered as only one of many factors and not the determining factor. It is therefore useless to hope that by artificially creating dependence of the bacilli in the human organism, their disappearance could then be caused by the withdrawal of the antibiotic.

G. M. Little

2123. Streptomycin Therapy in Laryngeal Tuberculosis

C. C. CODY. *Archives of Otolaryngology* [Arch. Otolaryng., Chicago] 53, 1-26, Jan., 1951. 12 figs., 43 refs.

This is an analysis of 16 cases of laryngeal tuberculosis—all with positive sputum and advanced pulmonary tuberculosis, and all except 3 with negative Kline and Kolmer reactions—treated with streptomycin, either alone or in combination with "sulfamylon", and either by nebulization or by parenteral injection.

The author accepts the figure of 20% to 30% for the incidence of laryngeal invasion in advanced phthisis, but remarks that this may be too low. On the whole, he thinks that invasion from the lung by the blood stream is the most probable route of infection, but that the effect of local trauma caused by coughing and expectoration should not be discounted; once local tissue resistance is broken down at such a "point of constant abuse" invasion by sputum-borne organisms is probable.

Until the advent of chemotherapy there has for 35 years been little change in the treatment of laryngeal tuberculosis. The incidence and severity of the disease have been reduced by better management of the pulmonary lesion (by collapse therapy, thoracoplasty, phrenicectomy, bronchoscopic treatment, and better methods of early diagnosis). For local treatment, diathermy, irradiation, and light therapy have all been reported as showing good results. Of the local surgical methods, electrocauterization had been giving better results with greater experience and, properly used in selected cases, was the treatment of choice before the discovery of streptomycin. Nerve block—of the superior laryngeal or glossopharyngeal nerve for pain, or of the recurrent laryngeal nerve on one side to put the part at rest—is palliative only and is not generally recommended. Amputation of the epiglottis seems to have no advantage over cauterization; tracheotomy and gastrostomy are desperate expedients.

In the present investigation 3 cases were treated with 0.2 g. of streptomycin 3-hourly; in all 3 patients the caloric response was lost and one had a 4-day erythematous rash, but stood smaller doses well. Another 6 patients had 1 g. in 4 doses of 0.25 g. each for 90 days; in 3 of these the caloric response was lost and a fourth patient had already lost the caloric response and had nerve-deafness (previous syphilis). This was the only case in which any deafness was noted. Probably in some cases of tuberculous laryngitis two-thirds to one-half of this dosage may be adequate. In 6 cases nebulized streptomycin was given with 5% sulfamylon hydrochloride, as sulfamylon is effective against organisms in a mixed infection which resist streptomycin and is more stable than penicillin in the mixture. One patient was given nebulized and parenteral streptomycin. This was the only case in the nebulized group where there was any loss of caloric response. In spite of this, parenteral therapy had a quicker and more certain action.

The great advantage of streptomycin treatment is in the relief of pain and the quick healing of granulation tissue. In most of the cases treated there was little or no effect on the lung; it is doubtful whether nebulized streptomycin alone can much influence the pulmonary condition.

F. W. Watkyn-Thomas

2124. Streptomycin Therapy in Urogenital Tuberculosis. (Zur Streptomycinbehandlung der Urogenitaltuberculose)

B. FISCH. *Zeitschrift für Urologie* [Z. Urol.] 44, 129-131, 1951.

On the basis of a brief experience the author concludes that in early cases of tuberculous cystitis benefit may be derived from streptomycin therapy, but that in cases of genital infection less favourable results are seen. In the latter operative treatment remains the method of choice. In recommending the small dose of 0.5 g. streptomycin (in 4 fractions given intramuscularly) daily up to a total of 20 to 40 g. the author claims never to have encountered the development of resistant organisms or the onset of vomiting or vestibular symptoms.

J. D. Fergusson

2125. Thiosemicarbazones in the Therapy of Tuberculosis. (Тиосемикарбазоны в терапии туберкулеза)

G. A. SUMBATOV. *Советская Медицина* [Sovetsk. Med.] No. 6, 6-9, 1951.

Clinical studies of thiosemicarbazones synthesized in the U.S.S.R. have been conducted in that country since 1949. Five such drugs have been under investigation in the author's laboratory since the end of that year. The present paper deals with two of them—"tibon" and "amitison". Both are known to have a bacteriostatic action on tubercle bacillus *in vitro* higher than that of *p*-aminosalicylic acid (PAS) and approaching that of streptomycin. Both have also proved their value in animal experiments; but they are highly toxic. Both tibon and amitison are powders insoluble in water or organic solvents. Administered by mouth they are rapidly absorbed and reach maximum concentration in the blood within the first 4 hours. Their presence in blood plasma can be observed 24 hours after a single

dose, and in the urine after 48 hours. Tibon combined with either PAS or streptomycin shows an increase in "bacteriostatic titre" in comparison with that of the two components taken individually. Animals suffering from tuberculosis have lower tolerance than healthy animals. Degenerative changes and loss of staining properties have been observed in tubercle bacilli from animals treated with tibon.

The present investigation included 178 patients treated with tibon and 89 treated with amitison; all except 3 were adults. The greater proportion of the patients were kept in hospital during the period of the treatment, but more than 80 of them had to undergo the later part of the treatment as out-patients. Treatment lasted from 1 to 8 months, and in 16 cases even longer. In 82 cases the tibon treatment had to be stopped either in view of toxic symptoms or deterioration in health, or simply because of absence of any improvement. Amitison produced a lower percentage of toxic effects, but as many as 41 cases out of 89 showed no improvement. Definite improvement was noted in 96 patients treated with tibon and 34 treated with amitison. It is probable that symptomatic improvement was, at least in part, due to rest and generally to the stay in hospital. Moreover, a few of the patients who showed definite improvement clinically as well as symptomatically had other forms of treatment as well. [The number of patients is not stated.] Four patients treated with tibon and 1 treated with amitison were discharged as cured; 49 treated with tibon and 14 treated with amitison showed definite improvement clinically.

The toxic effects of these two drugs were: weakness, headaches, vertigo, nausea and vomiting, pains in the stomach and in the region of the liver, insomnia, pruritus and itching skin eruptions, rhinitis, and conjunctivitis. More serious manifestations were occasionally observed: such as jaundice, transitory albuminuria, leucopenia and agranulocytosis, erythropenia, and a fall in haemoglobin level; in all these cases the treatment was discontinued.

The author recommends that the dose level of these drugs should be individually adjusted. The more ill the patient is, the smaller should be the initial dose. Temporary instructions issued by the Soviet Ministry of Health recommend 0.01 to 0.025 [? gramme] daily during the first week, up to 0.05 during the second and third weeks, and 0.1 to 0.15 daily subsequently.

In spite of their toxic effects, the author regards thiosemicarbazones as valuable agents in the treatment of tuberculosis and urges their further investigation.

A. Swan

2126. Effects of Adrenocorticotrophic Hormone and Cortisone in Patients with Tuberculosis

C. A. LEMAISTRE, R. TOMPSETT, C. MUSCHENHEIM, J. A. MOORE, and W. McDERMOTT. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 445-456, May, 1951. 9 figs., 10 refs.

Seven patients with advanced pulmonary tuberculosis were treated with ACTH or cortisone in an attempt to evaluate the participation of host mechanisms in tuberculous disease. In order that reliance should not be

placed entirely upon x-ray changes and other clinical factors which are difficult to assess, patients with active tuberculous laryngitis were included in the study. Each patient received 100 mg. of hormone intramuscularly in 4 equally divided doses at 6-hourly intervals for an initial 10-day period: 4 patients received ACTH and 3 cortisone.

During the period of administration of hormones rapid amelioration and subsequent disappearance of the constitutional manifestations of acute illness were witnessed. Patients became afebrile, but similar constitutional improvement was seen in 2 patients who were initially afebrile. In patients with laryngitis the symptoms abated at once, and subsequently the lesions were observed to become quiescent. Decrease in density of x-ray shadows was seen in 5 patients. Reversal of tuberculin skin sensitivity was observed in 3 out of the 6 patients tested.

On withdrawal of the hormone the signs and symptoms of acute illness rapidly returned and were as severe as or even worse than before. In the larynx, oedema and inflammation swiftly recurred on withdrawal of the hormones. The return of tuberculo-protein skin sensitivity was delayed for several weeks after cessation of hormone administration. Within 3 weeks after the completion of hormone treatment significant increases, both in concentration of serum gamma globulin and in the titre of tuberculous haemagglutinating antibodies, were noted in 3 of the 7 patients.

Further administration of hormones demonstrated that the improved state was temporary and could not be indefinitely maintained. In 2 patients with laryngitis complete healing occurred after the administration of streptomycin; the bacilli in these 2 cases were subsequently found to be streptomycin-sensitive. [The reaction of the group of patients as a whole to previous or subsequent streptomycin therapy does not emerge very clearly from the article, but the work was intended to evaluate the effect of the hormones given alone. It is pointed out that variations in the technique of hormone administration and the effect of their combination with other agents have yet to be evaluated.]

L. E. Houghton

2127. Indications and Contraindications for Tracheobronchoscopy in Patients with Pulmonary Tuberculosis.

(Показания и противопоказания для трахеобронхоскопии у больных легочным туберкулезом) A. A. LAPINA. Проблемы Туберкулеза [Probl. Tuberk.] No. 2, 29-33, March-April, 1951. 4 figs.

The views expressed in this paper are based on a series of 600 tracheobronchoscopies performed on adults, young children, and adolescents. There was not a single instance of activation of a latent tuberculous focus in larynx or lungs. The author stresses the importance of experience in this procedure, and the avoidance during bronchoscopy of force and pressure in passing the tube through the rima glottidis. Bronchoscopy was used in cases of pulmonary tuberculosis in which there were clinical signs and symptoms of disease of the trachea and bronchus, such as the presence of an obstinate, dry, spastic cough that failed to respond to treatment with

medicaments. Of 28 such patients 18 were found to have tuberculous infiltration and ulceration, and the remainder non-specific tracheo-bronchitis. Bronchoscopy was also performed on patients with tubercle bacilli in their sputum associated with one collapsed and one normal lung.

The author has observed the formation of obstructive atelectasis in patients after thoracoplastic operations, after induction of artificial pneumothorax, or as a result of obstruction of the lumen of a bronchus by thick sputum, by a tuberculoma in the main bronchus, or by caseous masses. Of particular interest from the author's point of view was the use of bronchoscopy in cases of cavitation of the lung where treatment by artificial pneumothorax had proved ineffective. In these cases all attention was directed to the treatment of the diseased and narrowed bronchus, and the progress of that treatment and the healing and disappearance of the cavity in the lungs were followed and confirmed by a series of tomograms.

Of 320 patients on whom bronchoscopy was performed 37 (11.1%) had tuberculous lesions of the main bronchi; these latter were mainly patients with cavernous forms of pulmonary tuberculosis treated ineffectively with artificial pneumothorax. In 20 cases radiological cure and disappearance of the tubercle bacilli from the sputum were observed.

In addition to the cases described, bronchoscopy was used in cases of haemoptysis of vague aetiology. Of 29 such patients it was found that 9 had carcinoma of the lung, 8 had bronchiectasis, and 4 had lung abscess. The contraindications to bronchoscopy in patients with pulmonary tuberculosis are given as: (1) the presence of tuberculosis of the larynx; (2) the presence of a far-advanced pulmonary tuberculosis accompanied by high temperature, dyspnoea, cyanosis, cachexia, or other signs of intoxication; and (3) the presence of aneurysm of the aorta, hypertension, decompensated heart disease, or mental disease. In conclusion the author says that bronchoscopy in patients with pulmonary tuberculosis may become, in experienced hands, a very useful diagnostic and therapeutic method.

I. Lopert

2128. Late Results of 225 Thoracoplasties Carried out in the Students' Sanatorium at Saint-Hilaire-du-Touvet from 1933 to 1948. (Résultats éloignés de 225 thoracoplasties d'indication pulmonaire faites au sanatorium des étudiants de Saint-Hilaire-du-Touvet de 1933 à 1948)

A. BONNIOT, D. DOUADY, R. COHEN, and P. BOSQUET. *Revue de la Tuberculose* [Rev. Tuberc., Paris] 15, 505-533, 1951. 1 fig., 1 ref.

In a total of 2,800 cases admitted to the hospital 225 thoracoplasties were performed on 221 patients who were mostly students, of both sexes, between 20 and 30 years of age. Of these, 219 were followed up at the end of 1950, with a maximum follow-up period of 16½ years, a minimum of 2½ years, and an average of 5½ years; 42% had up to four ribs removed, 35% five to six ribs, and 21% seven ribs; 30% had an apicolysis. The classification used was "dead", "not cured", and "cured", the criteria of cure being: (1) a radiograph showing healed

disease; (2) the absence of other foci of tuberculosis in the body; (3) a continued negative sputum on smear, and, in most cases, on guinea-pig inoculation; and (4) the pursuit of a normal life for some years. At the end of 1950, of the 221 patients 37 were dead (16.75%), 11 not cured (5%), and 171 cured (77.4%). Of the 171 cured 147 were cured by thoracoplasty alone, 9 by speliotomy associated with a thoracoplasty, and 15 by revision thoracoplasty.

The authors discuss bacteriological and radiological criteria of cure; they prefer radiological criteria. They found the latter criteria were satisfied in 6 months by 62 cases, in 6 months to 1 year by 46 cases, and in 1 to 2 years by 9 cases. These figures underline the importance of prolonged bed rest and a gradual return to active life after thoracoplasty. Of the 158 patients who returned to work, 64 did so between 1 and 2 years after the operation, 26 between 2 and 3 years, 14 between 3 and 5 years, and 4 after 5 years.

The results of thoracoplasty are studied in relation to various conditions, the prognosis depending on such pre-operative factors as the temperature, erythrocyte sedimentation rate, loss or gain in weight, size of cavity and amount of sputum. No prognostic value, however, could be attached to factors such as the extent of the lesion, whether it was bilateral or unilateral, or to the classic signs of retraction. The proportion of cures from thoracoplasty (77.4%) compared very favourably with the proportion of cures from all other methods of treatment used in the hospital in the same period, which was estimated to be less than 66%.

G. M. Little

2129(a). Artificial Pneumothorax: a Statistical Analysis of 557 Cases Initiated in 1930-1939 and Followed in 1949. I. The Influence of Clinical Findings before Induction on Early and Late Results

R. S. MITCHELL. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 64, 1-20, July, 1951. 47 refs.

This is one of an important series of studies all based upon the same 557 cases treated at Trudeau Sanatorium, New York, from 1930-39. It outlines the clinical material, the method of study, case selection, and end-results. The author does not attempt to evaluate pneumothorax, because of the known lack of satisfactory controls, but estimates the effect of various factors on the outcome of the procedure. It says much for the efficiency of the method of case recording that only 1% of cases were untraced, although the author had to depend upon questionnaires to former patients and to various institutions.

Each case was assessed at three points in the clinical course: (1) at one year after induction; (2) at abandonment of pneumothorax; and (3) at three years after abandonment. The result of each assessment was considered good when the following criteria were satisfied: (a) cavity closures seen in plain and stereoscopic chest radiographs; (b) clearing or contraction of infiltration; (c) no empyema; (d) no spread or increase in disease in contralateral lung; (e) sputum conversion on two or more consecutive concentrated-sputum smear examinations. Any failure to satisfy all the criteria was called a

poor result. The results were cumulative, and three years after abandonment was chosen by the author as the final point in the course, because, as he shows, this was the time when, in 249 patients, the evidence of post-abandonment reactivation of the disease reached its peak, and therefore it constitutes a fair test of complete healing.

The over-all results of pneumothorax treatment in this series of cases are given, but, as the author says, undue significance cannot be attached to them, since indications for, and practice of, the treatment varied markedly during this period of study. It is more instructive to study the pre-inductional clinical findings and their relation to the results. No variation in the results was found with place of induction, sex of the patient, the side on which the pneumothorax was performed, the trend of the lesion as judged clinically and radiographically, the size of the cavity, the thickness of the cavity wall as roughly estimated by radiographs, or the duration of rest in bed beforehand [but here the facts are less clear].

Late results were poor when the following factors were present: (1) increasing age of patient, poorest results occurring in patients 36 years of age or older; (2) increasing duration of the disease, as judged by the character and nature of the symptoms—these and the character of the radiographic appearance markedly affected the late results [no time limits are given]; (3) increased extent and density of the radiographic appearances; (4) evidence of endobronchial disease as shown by radiography, or the presence of tubercle bacilli in the sputum without evidence of cavitation (not upon endoscopic proof); (5) increasing extent and activity of the disease in the contralateral lung; (6) multiple cavitation.

John Sumner

2129 (b). Artificial Pneumothorax: a Statistical Analysis of 557 Cases Initiated in 1930-1939 and Followed in 1949. II. The Fate of the Contralateral Lung

R. S. MITCHELL. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 64, 21-26, July, 1951. 6 refs.

Reactivation of disease in the lung contralateral to pneumothorax was defined as any increase in disease necessitating treatment in hospital or at home, and it occurred in 135 cases out of the 557 studied during maintenance of the pneumothorax. Reactivation occurred much less often when the contralateral lung was normal before induction, but even so an incidence in normal lungs of 12.2% of all reactivations is astonishing; minimal lesions gave a slightly higher reactivation rate than advanced lesions. Active lesions of the contralateral lung were associated with a much higher reactivation rate. The extent of the lesions appeared to have no significance. The situation of the disease in the homolateral lung was unrelated to the incidence of contralateral reactivation. Reactivation was increased in the presence of dense radiographic shadows in the homolateral lung, but markedly diminished with complete anatomical freedom of the homolateral lung. Evaluation of the results of pneumothorax treatment is incomplete without a study of the fate of the contralateral lung.

John Sumner

2129 (c). Artificial Pneumothorax: a Statistical Analysis of 557 Cases Initiated in 1930-1939 and Followed in 1949. III. The Influence of Features of Management after Induction on Early and Late Results

R. S. MITCHELL. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 64, 27-40, July, 1951. 26 refs.

The materials, methods, and statistical criteria used, the definition of results, and the cases are described in Abstract 2129 (a). The author stresses that the value of the results shown is relative rather than absolute. The degree of freedom from pleural adhesions occurring either naturally or produced by adhesion section was the most important factor in the management influencing both early and late results. There is no doubt that complete anatomical freedom of the lung is most worthy of attainment; frequent thoracoscopy is necessary and should be performed as soon as possible after induction, so that abandonment and the institution of other forms of collapse therapy can be considered in patients with unsatisfactory collapse. Freedom from adhesions was a more important factor than cavity closure and sputum conversion.

Studying the results of pneumothorax in relation to duration of modified rest in bed, sanatorium residence, and time away from employment after induction, the author points out the difficulty in dissociating complicating features from those under study, and if more refined studies are made, the final number of cases is too small to give definite results either way. For similar reasons the relation of the duration of pneumothorax to late results is indecisive [perhaps the lack of adequate criteria for abandoning the pneumothorax is most important here]. It is suggested, however, that a 2- to 3-year pneumothorax gives as good a late result as a 4- to 6-year collapse. Cavity closure following a pneumothorax, as judged by radioscopes, simple radiography, and stereoscopic viewing, gave better late results if it occurred within the first four months and not later.

John Sumner

2129 (d). Artificial Pneumothorax: a Statistical Analysis of 557 Cases Initiated in 1930-1939 and Followed in 1949. IV. Incidence, Mortality, and Factors Associated with Complicating Tuberculous Empyema

R. S. MITCHELL. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 64, 127-140, Aug., 1951. 22 refs.

In this study tuberculous empyema was defined as a cloudy or purulent pleural fluid in which tubercle bacilli could be found by concentrated smear or culture examinations. No distinction is made between "pure" and "mixed" pleural infections, or between the absence or presence of a broncho-pleural fistula. In all, 605 cases were studied, including 48 from other series; some cases were excluded from the studies of certain points because of incomplete radiographs. Incidence of empyema during the period of 10 to 20 years after induction of pneumothorax was 18.2%. This figure, which is higher than that previously reported, may be due to the prolonged period of study. The mortality from empyema was greater the earlier the onset after induction, a peak occurring in the first year, with a tapering off about 3

years after the onset; the total mortality during the 10 to 20 years of study was 43.6%. The mean time interval between induction and onset of empyema was 24.5 months. The incidence of empyema was increased by the following pre-induction factors: (a) lack of rest in bed beforehand; (b) increasing age of patient over 34 years; (c) increased density of radiographic shadows in the collapsed lung; (d) increased thickness of the cavity wall. Post-induction factors in the increase of incidence were: (a) radiographic evidence of endobronchial disease soon after induction shown by the development of atelectasis; (b) delayed cavity closure and delayed sputum conversion [these two factors may be associated with the presence of endobronchial disease]; (c) lack of anatomical freedom of the lung.

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2129 (e) Artificial Pneumothorax: a Statistical Analysis of 557 Cases Initiated in 1930-1939 and Followed in 1949. V. Incidence, Degree, and Causative Factors of Pulmonary Contraction or "Unexpandable Lung"

R. S. MITCHELL. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 64, 141-150, Aug., 1951. 1 fig., 10 refs.

The author describes a crude method of estimating the extent of pulmonary contraction after pneumothorax, based upon a comparison of the radiographic size of the lung concerned before induction and after abandonment of the pneumothorax. He says that without complete physiological studies by bronchspirometry, lung volume determinations, and blood gas analyses the method used in the study can give only a rough estimate of the loss of pulmonary function following pneumothorax. Of 557 cases of pneumothorax, 312 were considered for this study. Of these 312 cases there was no contraction in 17%, total or nearly total contraction in 14%, and varying degrees of contraction occurred in the remainder. Empyema is the most important cause of pulmonary contraction. The following factors were found to be associated with some degree of pulmonary contraction: (a) increasing age of patient over 34 years; (b) increased duration of the pneumothorax over approximately 2 years, in both moderate and advanced lesions; (c) radiographic evidence of endobronchial disease either before or after induction. Factors not found to be associated with pulmonary contraction were: (a) the size of the cavity; (b) the location of the disease; (c) the trend of the disease; (d) the density of the radiographic shadows; (e) duration of bed rest before and after induction; (f) freedom from pleural adhesions; (g) the speed of cavity closure or of sputum conversion.

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2129 (f). Artificial Pneumothorax: a Statistical Analysis of 557 Cases Initiated in 1930-1939 and Followed in 1949. VI. Results in Various Selected Series of Cases

R. S. MITCHELL. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 64, 151-158, Aug., 1951. 7 refs.

This is the final report of this important series. By means of an ingenious method of selection and the exclusion of various factors shown to be associated with poor results or believed to be so associated on clinical

experience, the author confirms the evil effects of factors such as presence of endobronchial disease, lack of freedom from adhesions, and various other factors in combination. He is left with a few "golden rules" for the selection and management of cases for pneumothorax. [These indications for the treatment of pneumothorax are those which are now used in most modern institutions, and have been arrived at mainly on the basis of clinical experience; it is instructive to have them confirmed by this detailed statistical study.] These guiding rules are: (1) the radiographic shadows should be light, fluffy, and scattered, not dense, heavy, or confluent; (2) the extent of cavitation, the extent of presumed caseation, and the degree of contraction of old disease are more important than cavity size alone; (3) the location of the disease is not important; (4) contraindications are old fibroid disease, cavitation in the contralateral lung, any evidence of major bronchial obstruction; (5) at least 2 to 3 months' bed rest before induction, chemotherapy if indicated, and at least 3 months' bed rest after induction; (6) thoracoscopy to achieve good anatomical collapse will be necessary in at least 90% of cases, and if this is not obtained abandonment should follow; (7) atelectasis after induction or after adhesion section is a strong indication for abandonment; (8) cavity closure and sputum conversion should be obtained in 4 months; if not, abandonment should be considered; (9) duration of the pneumothorax should be measured from the date of cavity closure, sputum conversion, and the relief of symptoms, and should continue for 18 to 36 months, the exact time depending on the extent and the severity of the original lesion; (10) abandonment of the pneumothorax should be considered if fluid sufficient to cover the diaphragm persists for one month or longer, or if the fluid becomes cloudy or contains tubercle bacilli.

[Adherence to these rules for pneumothorax would limit its use; a study of the tables in this final report will, however, convince most that such a limitation is necessary in view of the rapid deterioration in results if the rules are not applied.]

John Sumner

See also Hygiene and Public Health, Abstract 1753; Pharmacology and Therapeutics, Abstract 1817; Radiology, Abstract 1847; Pathology, Abstracts 1873, 1875; and Microbiology, Abstract 1906.

PROTOZOAL INFECTIONS

2130. An Easier and More Accurate Diagnosis of Malaria and Filariasis through the Use of the Skin Scarification Smear

L. VAN DEN BERGHE and M. CHARDOME. *American Journal of Tropical Medicine* [Amer. J. trop. Med.] 31, 411-413, July, 1951. 3 refs.

After scarifying the skin of the scapular region smears of dermal juice are made and stained by the Giemsa method. By this technique both microfilariae and malarial parasites are found with greater frequency than they are in thick blood smear preparations.

J. L. Markson

2131. The Comparative Value of Amoebicidal Drugs

A. J. WILMOT, T. G. ARMSTRONG, and R. ELSDONDEW. *Journal of Tropical Medicine and Hygiene* [J. trop. Med. Hyg.] 54, 161-165, Aug., 1951. 6 refs.

Over 400 Africans with acute ulcerative amoebic dysentery were treated in groups of about 50 with one or other of 9 amoebicidal drugs in order to compare their curative action. The period of administration of a drug for assessing an "immediate cure" was 20 days. A group of 50 untreated cases served as a control. The following drugs were tested: emetine, "diodoquin" (diiodohydroxyquinoline), emetine bismuth iodide (E.B.I.), carbarsone, "yatren" (chiniofon), "militis" (bismuth *p*-N-glycolylarsanilate), "aralen" (chloroquine diphosphate), P 76 (phenyl diiodohydroxycinnamic acid), and P 196 (ethyl diiodohydroxycinnamic acid). The results are classified as "success", "possible failure", or "absolute failure", the first indicating absence of symptoms, ulcers, and amoebae; the second, some ulcers but no amoebae present; and the third, both ulcers and amoebae present. They are tabulated and analysed statistically.

Emetine, diodoquin, E.B.I., and yatren gave the best results and were about equally efficacious, with success in 50% or more; carbarsone gave success in 46% and absolute failure in 46%; while the remaining drugs showed very poor results. E.B.I. pills did not disintegrate in the bowel, and the authors advise that their manufacture should be discontinued forthwith. They point out that this paper records only a comparison of drugs used singly and is not a recommendation for individual therapy. [See also *Abstracts of World Medicine*, 1950, 7, 106; 8, 666.] J. F. Corson

2132. Laboratory Results on the Efficacy of Terramycin, Aureomycin and Bacitracin in the Treatment of Asymptomatic Amebiasis

J. E. TOBIE, H. MOST, L. V. REARDON, and J. BOZICEVICH. *American Journal of Tropical Medicine* [Amer. J. trop. Med.] 31, 414-419, July, 1951. 1 fig., 5 refs.

At an institution for mental defectives four infirmaries were selected for studies of the efficacy of terramycin, aureomycin, and bacitracin in the treatment of asymptomatic amoebiasis, all the patients in each of 3 infirmaries being given one of the three drugs, whether or not *Entamoeba histolytica* had been found in the faeces; the fourth infirmary was used as a control. Each group contained approximately 200 persons, and the prevalence rates for *E. histolytica* before treatment were as follows: terramycin-treated, 49%; aureomycin-treated, 45%; bacitracin-treated, 69%; untreated control, 64%. Patients weighing more than 75 lb. (34 kg.) were given 2 g. daily of terramycin or aureomycin, or 80,000 units of bacitracin; to those weighing under 75 lb. half of this dosage was given; treatment lasted 10 days. Patients with positive stools were studied at the end of a 2-week post-treatment period. Terramycin was 100% effective, aureomycin 100% effective, and bacitracin 59% effective. Six months later the apparent effectiveness of terramycin remained at 100%, while that of aureomycin fell to 60% and that of bacitracin to 28%. In the terra-

mycin-treated group the prevalence rate fell from 49% before treatment to 1% 6 months later.

While the efficacy of terramycin is clearly established, it is not, as a result of this study, considered to be superior to that of aureomycin. Terramycin appeared to have some effect against *Entamoeba coli* and *Endolimax nana*, and a more marked effect against *Iodamoeba bütschlii*.

J. L. Markson

2133. A Comparison of Aureomycin and Carbarsone in the Treatment of Intestinal Amebiasis

M. T. HOEKENGA. *American Journal of Tropical Medicine* [Amer. J. trop. Med.] 31, 423-425, July, 1951. 7 refs.

The comparative efficacy of aureomycin alone and a carbarsone-sulphadiazine combination was studied in Honduran patients suffering from intestinal amoebiasis. The finding of 6 negative stools over a 3-month period following treatment, together with cessation of symptoms, was taken as the criterion of cure. In 15 cases receiving 250 mg. aureomycin twice daily for 10 days the cure rate was 53%, and in 15 cases receiving 250 mg. aureomycin thrice daily for 10 days the cure rate was 80%; while in 40 cases receiving 250 mg. carbarsone thrice daily for 10 days and 5 g. sulphadiazine followed by 1 g. 4 times daily for 5 days the cure rate was 52%. Thus aureomycin in the higher dosage appears to be an effective amoebicidal drug.

J. L. Markson

2134. A Comparison of Chloroquine and Emetine in the Treatment of Amoebic Liver Abscess. [In English]

C. HARINASUTA. *Indian Medical Gazette* [Indian med. Gaz.] 86, 137-142, April, 1951. 6 refs.

The first 45 patients in this series of 90 treated for amoebic abscess of the liver in the Siriraj Hospital in Bangkok were given chloroquine. Starting with a loading dose of 0.6 g. by mouth, 0.3 g. was given daily for 12 to 19 days. Three patients died before adequate treatment could be given, and 3 of the 42 treated patients died. Relapse occurred in 10 of the 42 cases, though these patients responded to a second or, more rarely, a third course of treatment, one actually needing 5 courses. The drug was well tolerated and caused little side-effect, except in one patient through accidental and prolonged overdose, which caused epileptic convulsions. The second group of 45 patients received 9 daily injections of 1 gr. (65 mg.) of emetine. The usual toxic symptoms occurred but were only transitory, and one patient died. In both series aspiration was practised when deemed necessary, and open operation was resorted to in 18 of the 90 cases.

It is concluded that chloroquine possesses as great a curative action as emetine. In the present series it proved less toxic than emetine, though the relapse rate was higher. The author found that the length of treatment required was in proportion to the size of the abscess.

Clement Chesterman

See also Hygiene and Public Health, Abstract 1752; Pharmacology and Therapeutics, Abstracts, 1813 and 1809-10.